Development of Green and Sustainable Chemical Reactions

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Publication date:
2008

Document Version
Publisher's PDF, also known as Version of record

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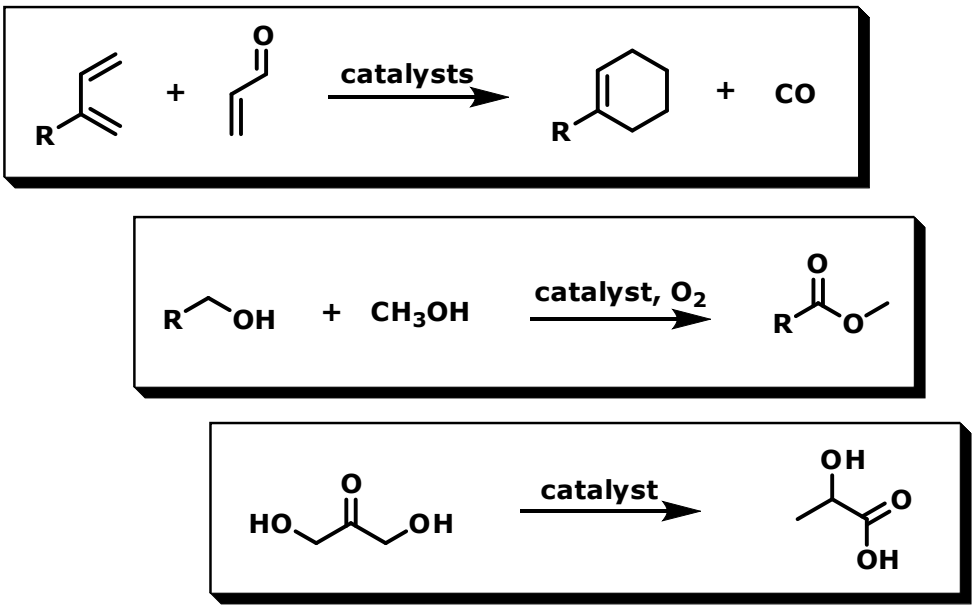

Esben Taarning

Ph.D. Thesis
Technical University of Denmark
Department of Chemistry
December 2008

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Preface

This thesis is submitted in fulfilment of the requirements for the Ph.d degree at the Technical University of Denmark (DTU). The work has been carried out at the Center for Sustainable and Green Chemistry (CSG) at DTU under the supervision of Professor Robert Madsen from September 2005 to November 2008. Some work has also been carried out at Osaka University under the supervision of Professor Kiyotomi Kaneda.

The objective of my Ph.d work has been to develop chemical processes that are both green and sustainable. The central strategy in my work has been to implement catalysis into new areas of chemistry. My work includes the development of a procedure in which α,β-unsaturated aldehydes are used as olefin synthons in the Diels-Alder reaction. I have also worked with the application of gold nanoparticles in the oxidation of alcohols and aldehydes, using oxygen as the stoichiometric oxidant. Finally, I have developed a process in which triose sugars can effectively be converted into polymer building blocks with the use of a heterogeneous catalyst.

I want to give my thanks and respect to Professor Robert Madsen for always taking the necessary time for in-depth discussions, and for giving me the opportunity to get involved in the areas of chemistry that I find most fascinating. Professor Claus H. Christensen deserves my thanks for giving me a broader view on chemistry and introducing me to heterogeneous catalysis. I also want to thank Professor Kaneda for his friendly and admirable personality and his dedicated supervision during my stay in his group.

I have worked together with many people who have contributed to my research during my Ph.d programme. Saravana Shunmugavel and Martin Spangsberg Holm deserve special mention here, as they through their insight into materials science and dedication have been priceless co-workers. I want to give a special thanks to Kresten Egeblad whom I have had the pleasure to work with during the last three years on many projects. Inger Staunstrup Nielsen and Anders Theilgaard Madsen have performed many of the experiments in the gold nanoparticle chapter and also have my greatest appreciation. I also want to thank all the people at CSG that I have been fortunate enough to know and to work with. Funding from the G.A. Hagemanns Memorial Foundation, the Augustinus Foundation and the Oticon Foundation for my external stay in the Kaneda group is greatly appreciated. Finally I wish to thank DTU for the Ph.d scholarship.

Abstract

This thesis entitled *Development of Green and Sustainable Chemical Reactions* is divided into six chapters involving topics and projects related to green and sustainable chemistry. The chapters can be read independently, however a few concepts and some background information is introduced in chapter one and two which can be helpful to know when reading the subsequent chapters. The first chapter is an introduction into the fundamentals of green and sustainable chemistry. The second chapter gives an overview of some of the most promising methods to produce value added chemicals from biomass as well as the possibility for establishing a renewable chemical industry is discussed.

The development of a procedure for using unsaturated aldehydes as olefin synthons in the Diels-Alder reaction is described in chapter three. This procedure affords good yields of the desired Diels-Alder adducts and only leads to small amounts of waste formation due to the all-catalytic nature of the procedure. This chapter involves the use of transition metal catalysis as well as classic organic chemistry.

In chapter four, supported gold nanoparticles are used as catalysts for the aerobic oxidation of primary alcohols and aldehydes to afford methyl esters directly. The developed procedure is applied to several substrates that can be made from biomass resources and as a result, some new biomass derived products are made available using gold nanoparticle catalyzed oxidations.

In chapter five the development of a procedure for converting triose sugars into lactic acid and methyl lactate is described. Conventional and Lewis acidic zeolites are used as catalysts for this transformation and this procedure illustrates how zeolite catalysis can play an important role in the production of value added chemicals from biomass. Finally, a brief summary and outlook is given in chapter six.

Resumé

Denne afhandling med den danske titel *Udvikling af grønne og bæredygtige kemiske processer* er opdelt i seks kapitler, som handler om emner og projekter vedrørende grøn og bæredygtig kemi. Kapitlerne kan læses uafhængigt af hinanden, men der introduceres dog nogle begreber og noget baggrundsstof i kapitel et og to som kan være behjælpelige at kende til i de senere kapitler. Det første kapitel er en introduktion i bæredygtig og grøn kemi. I kapitel to gives et overblik over nogle af de vigtigste og mest lovende metoder til at fremstille værdiforøgede kemikalier fra biomasse, og samtidig diskuteres muligheden for at opbygge en kemisk industri baseret delvist på fornybare resurser.

I kapitel tre beskrives udviklingen af en metode hvori umættede aldehyder kan bruges som oelfin-synthoner i Diels-Alder reaktionen. Med brug af denne metode kan gode udbytter af det ønskede Diels-Alder addukt opnås og samtidig dannes der kun små mængder affald under reaktionen idét metoden udelukkende gør brug af katalytiske værktøjer. Dette kapitel omfatter brugen af overgangsmetalkatalyse samt mere klassisk organisk kemi.

I kapitel fire bruges guldnanopartikler som katalysatorer til oxidation af primære alkoholer og aldehyder med luft til fremstilling af methylestre. Den udviklede metode er anvendt på adskillige substrater som kan produceres fra biomasseresurser hvilket resulterer i at en hel ny række produkter kan skabes fra biomasse ved brug af guldnanopartikel-katalyse.

I kapitel fem beskrives udviklingen af en metode til at omdanne triose-sukre til mælkesyre og methyl laktat. Konventionelle og Lewis-sure zeolitter bruges som katalysatorer i denne omdannelse og metoden illustrerer vigtigheden af zeolit-katalyse i produktionen af værdiforøgede kemikalier fra biomasse. Endelig gives til slut en kort opridsning i kapitel seks.

Publications included in the appendix

1. C.H. Christensen, J. Rass-Hansen, C.C. Marsden, E. Taarning, K. Egeblad, **The Renewable Chemicals Industry**, *ChemSusChem*, **2008**, *1*, 283.

2. K. Egeblad, J. Rass-Hansen, C.C. Marsden, E. Taarning, C.H. Christensen, **Heterogeneous Catalysis for Production of Value-added Chemicals from Biomass**, *in Catalysis – vol. 21*, **2008**, Ed. J.J. Spivey, RSC Publishing 2008.

3. E. Taarning, R. Madsen, **Unsaturated Aldehydes as Alkene Equivalents in the Diels-Alder Reaction**, *Chem. Eur. J.*, **2008**, *14*, 5638.

4. E. Taarning, C.H. Christensen, **Gold Nanoparticle Catalyzed Oxidation of Alcohols: From Biomass to Commodity Chemicals**, *Chimica Oggi-Chem. Today*, **2007**, *25*, 70.

5. I.S. Nielsen, E. Taarning, K. Egeblad, R. Madsen, C.H. Christensen, **Direct Aerobic Oxidation of Primary Alcohols to Methyl Esters Catalyzed by a Heterogeneous Gold Catalyst**, *Catal. Lett.*, **2007**, *116*, 35.

6. E. Taarning, I.S. Nielsen, K. Egeblad, R. Madsen, C.H. Christensen, **Chemicals from Renewables: Aerobic Oxidation of Furfural and Hydroxymethyl Furfural over Gold Catalysts**, *ChemSusChem*, **2008**, *1*, 75.

7. C. Marsden, E. Taarning, D. Hansen, L. Johansen, S.K. Klitgaard, K. Egeblad, C.H. Christensen, **Aerobic Oxidation of Aldehydes under Ambient Conditions using Supported Gold Nanoparticle Catalysts**, *Green Chem.*, **2008**, *10*, 168.

8. E. Taarning, A.T. Madsen, J.M. Marchetti, K. Egeblad, C.H. Christensen, **Oxidation of Glycerol and Propanediols in Methanol over Heterogeneous Gold Catalysts**, *Green Chem.*, **2008**, *10*, 408.

9. E. Taarning, S. Saravanamurugan, M.S. Holm, J. Xiong, R. West, C.H. Christensen, **Zeolite-catalyzed Isomerisation of Triose Sugars**, *submitted*.

Miscellaneous publications

S.K. Klitgaard, K. Egeblad, U.V. Mentzel, A.G. Popov, T. Jensen, E. Taarning, I.S. Nielsen, C.H. Christensen, **Oxidations of Amines with Molecular Oxygen using Bifunctional Gold-Titania Catalysts**, *Green Chem.*, **2008**, *10*, 419.

B. Jørgensen, E. Taarning, C.H. Christensen, **Den fornybare kemiske industri,** *Dansk Kemi*, **2007**, *88*, 26.

E. Taarning, T. Jensen, J.H. Dam, R. Madsen, **Industriel organisk kemi**, *Nye Kemiske Horisonter, DTU*, **2007**, 88.

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1. Green and Sustainable Chemistry

Chemistry constantly thrives towards fulfilling new and existing demands from consumers and end users. This has been the case for at least a century, where medicines, pesticides, high-performance materials and many other products have been developed and integrated into our society. New demands constantly arise and forces chemistry to adapt. One of which is the desire to minimize our environmental footprint on the planet. This has led to the coinage of terms such as *green and sustainable chemistry*.

Sustainable development has been described as *development that meets the needs of the present generation without compromising the ability of future generations to meet their own needs* [1]. Green and sustainable chemistry therefore encompass many research areas, such as design of processes that utilize resources efficiently, sustainable resource management, the reduction of waste and hazardous chemicals, the use of safe chemicals and much, much more. Green and sustainable chemistry is currently receiving increasing attention since it could hold the key for solving three major challenges that are becoming more and more urgent, namely the resource challenge, the climate challenge and the environmental challenge.

1.1 The resource challenge

The resource challenge is a result of the global population boom of the 20th century, where the population has almost quadrupled to over 6 billion people by the year 2000. This, combined with the fact that more and more people enjoy the benefits of a high living standard, has put strain on the resources needed to fuel this population and consumption boom (figure 1). Chemistry has made a vast array of materials, medicines, fertilizers and fuels available at low cost. However, the chemical industry is based almost entirely on processes that convert petroleum derived resources into these highly valued products. During most of the 20th century, cheap and abundant petroleum feedstocks have been readily available; however it has become shockingly clear that these feedstocks will be priced very differently in the 21st century, as the dwindling supplies can no longer keep pace with an ever increasing demand. This event will undoubtedly impact the chemical industry of the 21st century.

1.1.1 Energy resources

The global energy demand is in constant growth (figure 2). But whereas electricity can be generated in many ways, using many types of resources (coal, gas, oil, solar, nuclear, wind, biomass,

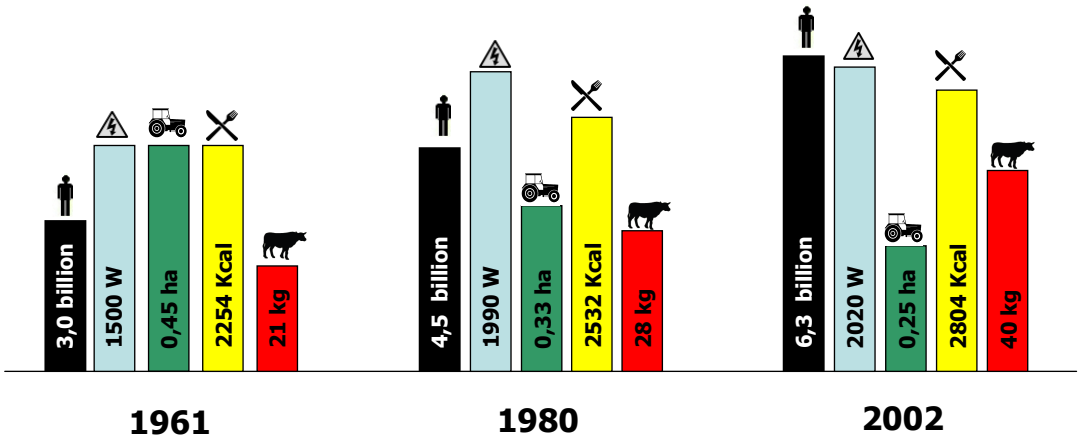


Fig. 1 Data showing the development of the global population during the last half of the 20th century and per capita development in energy use, arable land, calorie intake and annual meat consumption (from left to right) [2-3].

hydroelectric, wave, *etc*.) transportation fuels have traditionally been obtained most economically from oil. The energy challenge thus has two major components; sustainable electricity generation and sustainable transportation fuel generation.

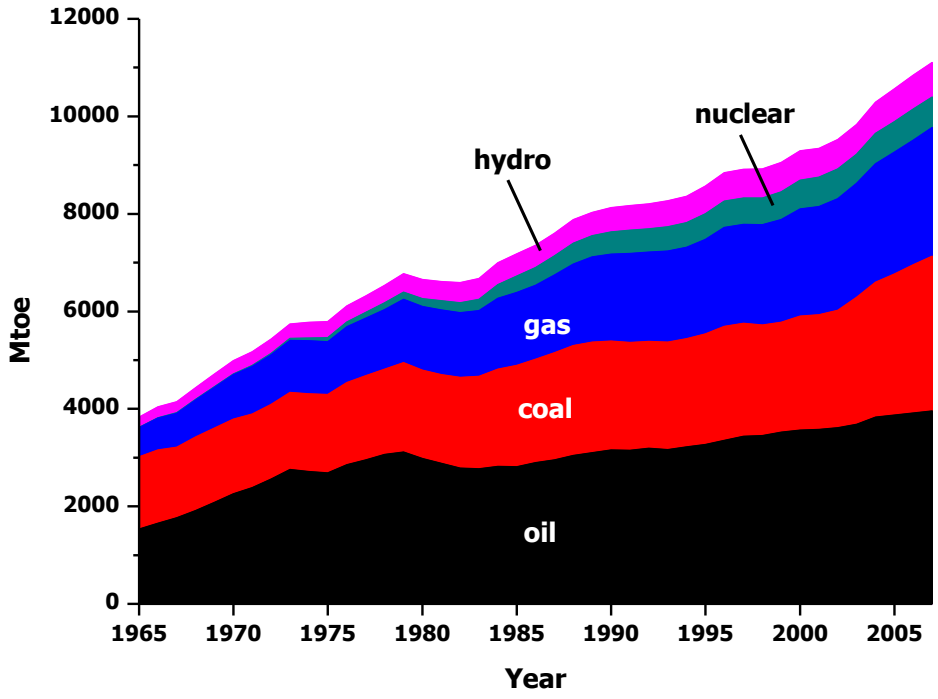


Fig 2. Development in the global energy consumption measured in million tonnes of oil equivalents (Mtoe) [3].

Electricity generation is therefore from a resource point of view a separate challenge from transportation fuel generation, since coal reserves are believed to last for hundreds of years at the current consumption rate. Furthermore, technologies that enable sustainable energy generation are already in existence. The major drive for sustainable energy generation lies in the concern that the vast amounts of carbon dioxide released from coal generated electricity will affect the global climate as well as the desire to be less dependent on energy supplies from foreign nations. Transportation fuel generation is, on the other hand, a more imminent matter since the production of oil is believed by many to have peaked or peak in the near future [4]. However, several alternatives to refining oil exist. Coal and biomass can *e.g.* be converted to liquid fuels by gasification followed by Fischer-Tropsch synthesis and carbohydrates can additionally be fermented to ethanol.

1.1.2 Biomass

Biomass is a general term for resources which are annually renewable. It is made by the fixation of carbon dioxide via the photosynthesis to produce carbohydrates. In other words, sunlight is used for the reduction of carbon dioxide with water to form a solid carbonaceous biomass material that can be harvested. In this process, up to 1% of the energy content of the sunlight can be stored in the carbohydrates. The annual fixation of carbon by terrestrial plants is around 57 billion tonne. The majority of which is fixated as carbohydrates and to a less degree (around 25%) as lignin. A large portion of this is released back into the atmosphere by wildfires and natural decomposition. Another 57 billion tonne is fixated in the ocean. Annually, a staggering amount of 7.7 billion tonne of carbon (2005) is released into the atmosphere by human combustion of fossil resources [5]. The amount of harvestable carbon fixated in croplands is less than this, amounting to 7 billion tonne. In other words, all the harvested biomass (corn, straw, wheat, *etc*.) contains too little carbon to fully substitute the fossil carbon that is currently used. Furthermore, biomass carbon is in a higher oxidation state than fossil carbon in the form of hydrocarbons. This means that combustion of biomass carbon will produce less energy than fossil carbon in general, further expanding the gap between fossil resources and biomass resources. It thus seems apparent, that if biomass resources should fully replace fossil resources, a substantial increase in the capacity of the agricultural sector is needed. This adds new complications, since an increase in the agricultural sector will further increase the demand for fossil resources (transportation fuels, fertilizers, *etc*.), not to mention the impact of extensive energy-farming on global food prices. This simple calculation also does not take the energy loss of converting biomass to liquid fuels into consideration.

1.1.3 Mineral resources

Oil is not the only resource that is running short in the not so distant future. Excessive mining of minerals will ultimately lead to depletion of many easily accessible reserves. Phosphate in the form of easily accessible phosphate rock is used in very large quantities as fertilizer in the agricultural sector. Some argue that phosphate rock production has peaked and that availability of phosphate could become a limiting factor for the agricultural sector in the future [6]. Many metals are also likely to be depleted in just a few decades at the current consumption rate, in particular rare metals such as indium, tantalum and hafnium which are used in LCD monitors and electronic components. Metals such as lead, copper and aluminium are also believed to run short in the 21st century [7]. The oil and mineral deposits which are easiest to access are generally utilized prior to using the more hard-to-come-by deposits, for obvious economic reasons. This means that the cost of extracting a resource is expected to increase as it is being depleted as well as the cost of refining a less pure grade of metal ore is higher. Therefore the consequence of depleting these resources will in the end be that the price of consumer goods will increase. The consequence of depleting the phosphate mineral deposits will be direr, as this could result in a more inefficient agricultural sector and thus an increase in food prices and a poor prospect for energy farming.

1.1.4 Outlook for a sustainable resource management

Sustainable transportation fuel generation is without a doubt the greatest component of the resource challenge, simply because of the sheer amount of fuel needed. It seems that there is no single key to solve this challenge, but rather many different approaches are needed. Biofuels can perhaps supply 30% of the current fuel demand if fully developed [8]. Hybrid cars can help to lower fuel consumption in many areas and technologies such as fuel cells could also lower the need for liquid fuels. These approaches, however, all have their own drawbacks. Biofuels demand large areas of arable land, batteries for hybrid cars require electricity and expensive metals and fuel cells require significant amounts of rare metals such as platinum. The non-sustainable conversion of coal to liquid fuels is therefore likely to become a very important source of fuel in the future. However, it seems possible that the cost of transportation will increase in the future as a result of a more strained fuel situation.

In order to maintain our high living standards, new ways of managing our resources will be necessary in the future. Recycling is bound to play a larger role than it currently does and reuse of

metals and fertilizers will most likely be a key element in achieving a more sustainable resource management. However, new technologies by which metals can be replaced with non-metal components, such as plastics, organic light emitting diodes, organic semi-conductors and conductors could be a more sustainable approach in the long run. Furthermore, biofuels are likely to be a significant part of our fuel supply in the future, but they are unlikely to fully substitute fossil fuels at our current consumption rate. No matter what the solution will be, chemistry is bound to play a key role in facing this challenge.

1.2 The climate challenge

The continuous use of fossil resources has resulted in a climate challenge due to the build up of carbon dioxide in the atmosphere. Since the start of the industrialization, the CO_2 level has increased from 280 ppm to a current level of 384 ppm, growing around 2-3 ppm annually. Although still up for debate, most climatologists believe that these elevated levels will result in an increased average global temperature. This event could bring about unforeseeable changes to the climate. Therefore, greenhouse gas reduction has received tremendous attention, both scientifically and politically.

1.2.1 Efficient use of biomass

Many different steps towards reducing our CO_2 emissions or simply reducing the growth of our emissions have been undertaken. Some of these steps are well-known and include the use of wind, solar, geothermal, hydro and nuclear power.

Biomass can be used for generating CO_2-neutral electricity through combustion in power plants, which probably represents the most CO_2-effective use of it. However, biomass can also be used for other purposes such as transportation fuel generation and the production of chemicals. Since production of biofuels can help reduce our dependence on oil, this has become an attractive alternative. From a climate point of view though, biofuel production from sources such as corn does not lower the overall CO_2 emissions significantly, as a large energy input is needed in the conversion process [9]. It is possible however, that biomass can be used more efficiently for the production of some chemicals and thereby still help to reduce our dependence on oil [10]. This is possible if selective removal of functionality can be done more cost effectively than the addition of functionality to unfunctionalized petrochemical feeds. However, this approach requires that many

new transformation reactions for biomass are developed and thus again appeals to chemists to play a role in facing this challenge.

1.3 The environmental challenge

Since chemical processes create waste, management of this waste is an important issue. Generation of waste can be viewed as an inefficient use of resources that will consequently result in a less economically attractive process. The most attractive way to manage waste is therefore to prevent it rather than to clean it up.

1.3.1 Atom economy

The E-factor has been introduced by Roger Sheldon as a tool to evaluate the environmental impact of a particular reaction, based on how much waste is generated [11]. The E-factor is defined as the waste-to-desired-product weight ratio. A reaction in which no waste is generated thus has an E-factor of 0. This is a very crude but simple way to compare the waste generation of similar types of reactions. Table 1 compares typical E-factors from various segments of the chemical industry, and as can be seen, production of bulk chemicals is highly efficient compared to production of fine chemicals and pharmaceuticals.

Industry segment	Annual tonnage	E-factor
Oil refining	10^6-10^8	< 0.1
Bulk chemicals	10^4-10^6	<1 to 1
Fine chemicals	10^2-10^4	5-50
Pharmaceuticals	10-10^3	25-100

Table 1. E-factors for different segments of the chemical industry [11].

This large difference in waste generation can be explained in part by a wider use of catalysts for large scale reactions. A catalytic process which uses hydrogen as a reducing reagent is necessarily much more atom efficient than a process using *e.g.* a hydride reducing agent. A comparison of the E-factors for different oxidants can be seen in table 2. Obviously, the E-factor obtained from using oxygen (O_2) as the oxidant is lower than using traditional oxidations and one may even argue that water is not really a by-product in the same way as *e.g.* manganese waste. But perhaps most

interestingly from an economic point of view is that oxygen is free when used in the form of air. However, in order to use oxygen as an oxidant a catalyst is necessary. A key area in green chemistry is therefore to develop catalytic processes that enable the use of the simplest reagents and are reliable enough to be widely used for the production of fine chemicals and pharmaceuticals.

Oxidant	E-factor
Dehydrogenation	0.02
O_2	0.18
H_2O_2	0.37
$KMnO_4$	1.10
$NaIO_4$	2.20
Dess-Martin periodinane	4.35

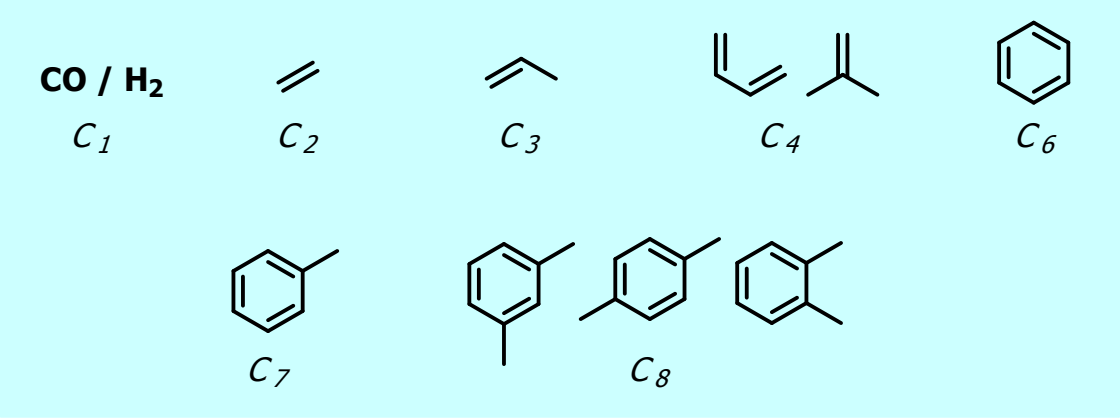
Table 2. E-factors for the oxidation of cyclohexanol with different oxidants assuming 100% yield.

1.4 Outlook

With the important role of chemistry in mind, the stage is now set to discuss the potential for a chemical industry based in part on the use of biomass as feedstock for the production of chemicals. This is topic is discussed in chapter 2. Chapter 3 describes the development of a procedure to use α,β-unsaturated aldehydes as atom economic olefin synthons for the Diels-Alder reaction. Chapter 4 deals with gold nanoparticles for the aerobic oxidation of alcohols. Finally, chapter 5 describes the development of a new process for converting biomass into biodegradable polymer building blocks.

2. The Renewable Chemical Industry

The chemical industry is a mature and highly optimized industry which is predominately based on the conversion of petroleum feedstocks into value added chemicals. Seven building blocks that are easily produced from oil and gas are converted via a plethora of chemical reactions into the vast number of consumer products that are used [12]. These seven building blocks are shown in scheme 2.1 and consist of syngas (C_1), ethylene (C_2), propylene (C_3), the butenes (C_4), benzene (C_6), toluene (C_7) and xylenes (C_8).



Scheme 2.1

Since fossil feedstocks are mainly composed of aliphatic and aromatic hydrocarbons, the key goal in the valorization lies primarily in the separation of different compounds, which is typically done by distillation, followed by functionalization of the unfunctionalized compounds. One example of this is the hydrogenation of benzene to cyclohexane and oxidation of cyclohexane to a mixture of cyclohexanol and cyclohexanone with air using a cobalt catalyst. Final oxidation of the cyclohexanol/cyclohexanone mixture by nitric acid affords adipic acid which is used for the production of nylon [13]. This is one of many examples in which the overall strategy is valorization through functionalization. Figure 2.1 show some of the most important products and the annual volume of these that are produced from the seven building blocks using this overall strategy.

2.1 Chemicals from biomass

Carbohydrates constitute the most important group of renewable resources due to their high abundance. Glycerol is another important renewable resource which is produced as a by-product from the production of biodiesel. When discussing these bio-resources, it is important to keep their

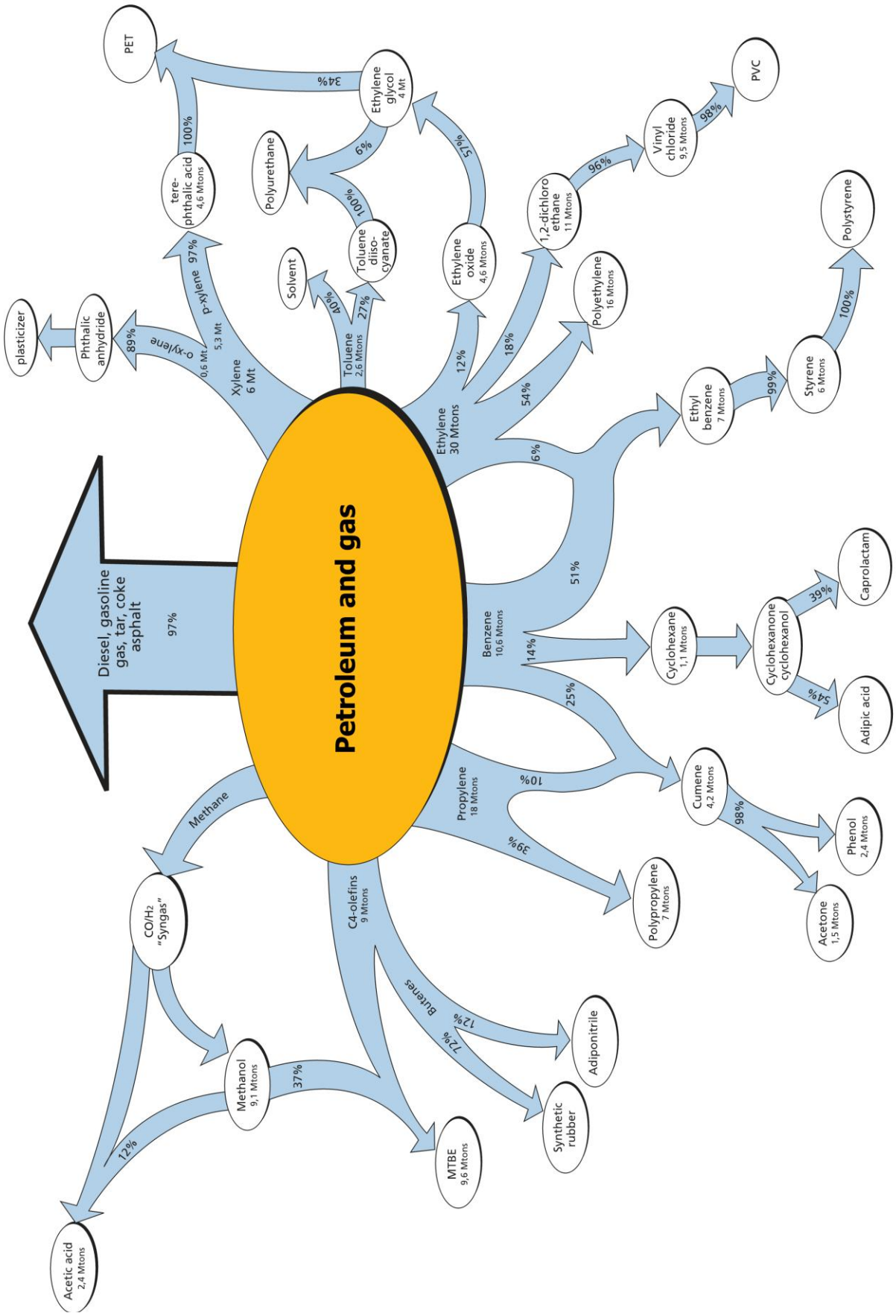


Figure 2.1 A rough overview showing the most important pathways for the production of organic chemicals. The volumes are based mainly on data from Industrial Organic Chemicals by Wittcoff, Reuben and Plotkin [12].

relative volumes in mind. The current annual production of biodiesel is around 11M tons globally, leading to the by-production of little more than 1M tons of glycerol. This number dwindles in comparison to the total annual production of carbohydrates in the biosphere of around 135.000 M tons or roughly 75% of the entire biomass production, and underlines the importance of this class of molecules [14]. Around 5% of this is harvestable and the rest decays by natural pathways. Due to the complexity of biomass and the high degree of functionality, the overall strategy with biomass valorization is to remove functionality in a selective manner. This is directly opposite to petroleum refining and different in many aspects. The first and most obvious difference is that carbohydrates are solids. They therefore have to be processed in a solvent, preferably water, if selective chemical transformation reactions are to be carried out since carbohydrates tend to decompose non-selectively in the absence of a solvent. Secondly, carbohydrates do not tolerate the high temperatures that are often used for petroleum refining. It is therefore obvious that the tools used for petroleum valorization are not applicable for the valorization of biomass.

The conversion of glycerol and carbohydrates to value added chemicals has been the subject of intense study and several literature reviews and books on this topic have been published. Since it would be pointless to make a complete literature overview of this area, a short list of some of the more recent and important reviews will have to suffice. Corma *et al*. have perhaps made the most thorough review, listing many important chemical intermediates from biomass and chemical processes for transforming these to useful chemicals [15]. Christensen and co-workers have surveyed the field of heterogeneous catalysis in biomass conversion on a reaction-type basis [16] and also described the possibility of basing a chemical industry on biomass using both biochemical processes and conventional catalysis [10]. Werpy and Petersen have made a thorough report for the US Department of Energy, narrowing down the twelve most important renewable building blocks as well as the obstacles that are associated with their implementation (table 2.1) [17]. The use of glycerol for the production of value added chemicals has been reviewed by Pagliaro *et al.* [18]. However, these examples only constitute the tip of the ice berg in the biomass-to-chemicals research area. The rest of this chapter is devoted to illustrate some of the overall trends and strategies that are being pursued in the valorization of carbohydrates and glycerol.

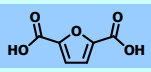
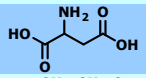
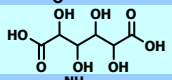
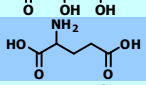
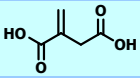
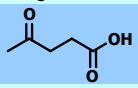
Chemical	Source	Method
succinic acid, fumaric acid, maleic acid	sugars	fermentation
2,5-furan-dicarboxylic acid 	C_6 sugars	dehydration
3-hydroxy-propionic acid	sugars	fermentation
aspartic acid 	fumaric acid	fermentation or amination
glucaric acid 	starch	oxidation
glutamic acid 	sugars	fermentation
itaconic acid 	sugars	fermentation
levulinic acid 	C_6 sugars	dehydration
3-hydroxybutyrolactone	starch	oxidation
glycerol	triglycerides	transesterification
sorbitol	C_6 sugars	hydrogenation
Xylitol/arabinitol	C_5 sugars	hydrogenation

Table 2.1 The twelve most important chemicals that can be made from renewables according to Werpy and Petersen [17].

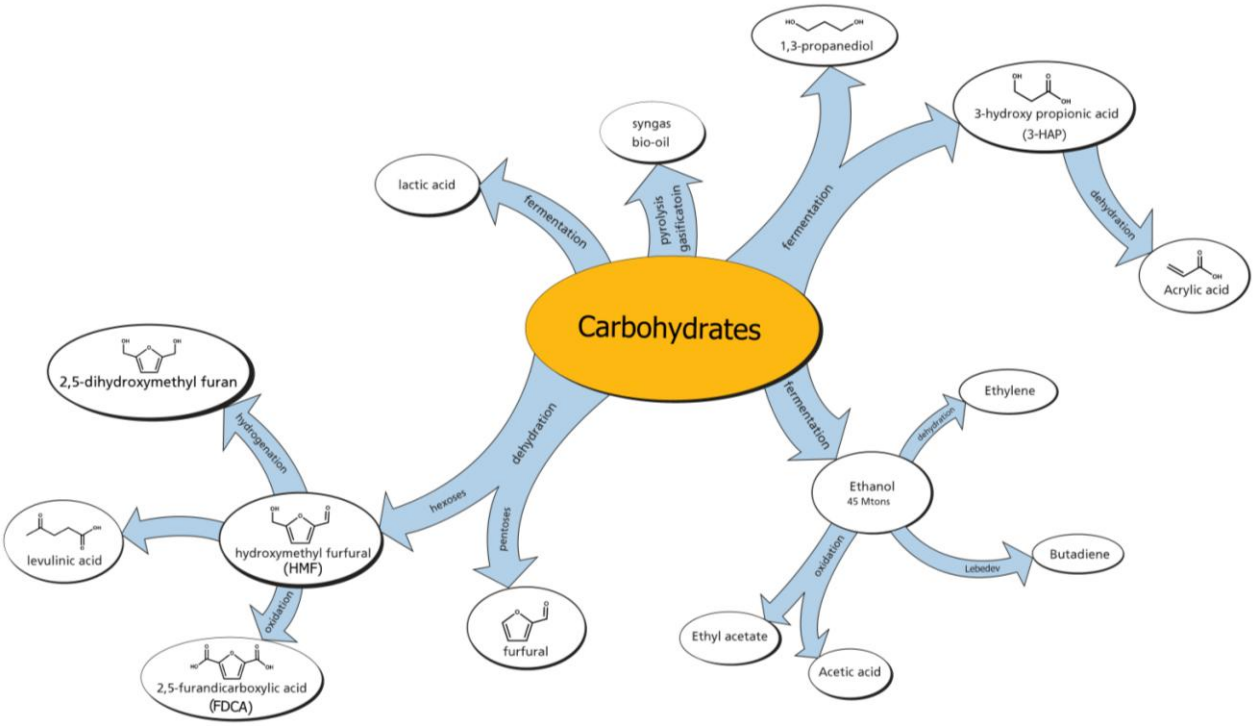
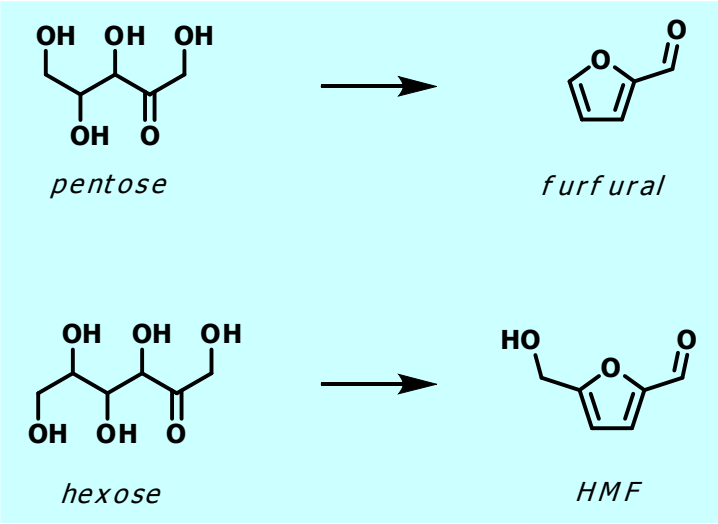


Figure 2.2 shows some of the most important and most studied examples of chemicals that can be produced from carbohydrates, either directly or indirectly.

2.2 Carbohydrates – the chemist's approach

From a conventional catalytic standpoint the major obstacle with carbohydrates as a chemical feedstock is its complexity and thermal instability. A central goal in using a conventional catalytic approach for converting carbohydrates is therefore to remove some of this complexity and thereby make the feedstock more thermally stable. Defunctionalization is thus a central issue if selective conversion has to be achieved by chemical means. In order to achieve this, one of the most useful approaches is to dehydrate the carbohydrates using a catalyst. Catalytic dehydration is both a green and economically friendly transformation type since it does not require the use of any external reagents.

Hemicellulose is a sugar polymer that is present in plant material in large amounts. Unlike cellulose, it can easily be hydrolysed to sugar monomers by acid hydrolysis. A major sugar component in hemicellulose is the C-5 sugar xylose. This makes xylose a highly abundant sugar which could be an interesting feedstock for the production of chemicals. Dehydration of xylose to

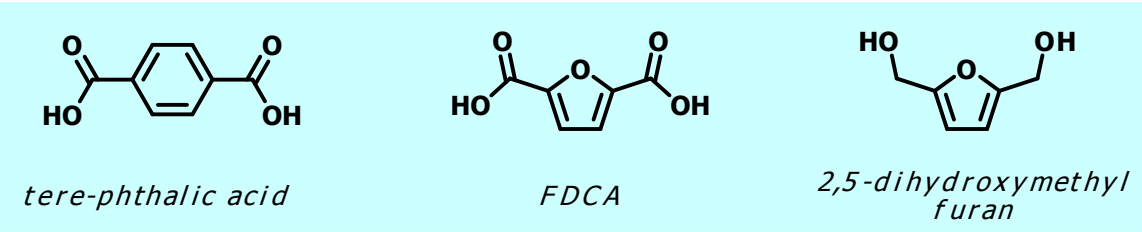


Scheme 2.2

produce furfural (scheme 2.2) was employed as early as 1922 by the Quaker Oats Co by reacting corn hobs in the presence of aqueous sulfuric acid and steam-distilling furfural from the mixture [19]. One advantage of producing a volatile product directly from carbohydrates is that the purification can be easily accomplished by distillation. Furfural itself has, however, only found limited use as an industrial extractant, but via decarbonylation over a supported palladium catalyst and subsequent hydrogenation it is transformed to THF, an important solvent that finds widespread

use [20, 21]. Mineral acids have traditionally been used for this dehydration reaction but more recently acidic zeolites have, among other catalysts, been demonstrated to work equally well [22-23]. The use of acidic zeolites makes purification easier and typically the zeolite can be reused many times. The temperature range for the dehydration reaction is typically in the range of 140-170 ºC, which is a quite common temperature range for dehydration of carbohydrates, and typical yields of furfural of 80% can be achieved.

Dehydration of hexoses to form another furan derivative, namely 5-hydroxymethyl furfural (HMF), has received tremendous attention recently [24, 25]. The main reason for this is that by oxidation or hydrogenation, HMF can be converted to 2,5-furandicarboxylic acid (FDCA) or 2,5-dihydroxymethyl furan, respectively [26, 27]. Both these compounds have an inherent bi-functionality, which allows them to be used as polymer building blocks in much the same way as *e.g.* tere-phthalic acid [25] (scheme 2.3). Thus, in very few steps it seems to be possible to transform readily available carbohydrates into high value chemicals useful for making plastics.



Scheme 2.3

Several obstacles exist when making HMF. First of all, only fructose can be dehydrated with high selectivity to give HMF. Due to its higher price, fructose is a less attractive feedstock than the cheaper glucose. Secondly the dehydration process is often hampered by complications which are related to the instability of HMF under the conditions at which it is formed. Under acidic aqueous conditions HMF tends to rehydrate and ring-open to form levulinic acid. This has the overall implication that at high fructose conversions the HMF selectivity becomes low. To minimize this complication, processes utilizing continuous extraction of HMF with an organic solvent from the acidic aqueous phase have been developed [28]. Here, HMF has been reported to be formed with 89% selectivity at 95% conversion and interestingly glucose can also be transformed to HMF with 47% selectivity at 50% conversion using this type of process. An equally interesting approach has been to oxidize HMF to FDCA as it is formed. FDCA is acid stable, and can be formed in one-pot

by the use of a bi-functionalized catalyst capable of catalyzing both the dehydration reaction to form HMF and aerobic oxidation of HMF to FDCA [29]. The use of ionic liquids as solvents for the formation of HMF has also been reported. Here, many options for designing an effective reaction media are available and yields of HMF up to 70% starting from glucose have been reported [30]. However, even though many different methods for forming HMF are described in literature, a large scale commercial process has yet to be implemented.

FDCA is not the only interesting product that can be made from HMF. For instance it has been demonstrated that HMF reacts with acetone in an aldol reaction to form C9 and C15 compounds. By subsequent hydrogenation this mixture can be transformed into gasoline and diesel, thereby opening up for a non-enzymatic transformation of carbohydrates to transportation fuels [31].

2.2.1 Carbohydrates – fermentation

Countless of biological processes exist in which carbohydrates are transformed into interesting chemicals. Some of these processes can become useful tools in the valorization of carbohydrates. One benefit of using biological processes is that mild reaction conditions are usually employed whereby the troublesome thermal instability of carbohydrates is no longer a complication. Furthermore it is often possible to produce chemicals which would not have been accessible to produce with a traditional chemical approach. Ethanol is *e.g.* easily obtainable from glucose by fermentation, whereas it is difficult to imagine an efficient route using conventional catalysis. However, biological processes also have many obstacles that have to be faced and weighed against the use of conventional catalysis. The main obstacle is related to the fact that often a very narrow set of reaction conditions must be used, such as a limited pH-range, the need for nutrient additives, long reaction times and product inhibition. Furthermore, product purification in a biological process is often expensive since low product concentrations are typically obtained and the removal of excessive amounts of water is highly energy consuming. Much of the on-going research in this direction is related to the construction of genetically modified bacteria or fungi, *e.g.* by switching off or enhancing a specific reaction pathway, resulting in the accumulation of a desired chemical product [32].

Fermentation of glucose to ethanol is one of the largest industrial processes in operation today. Annually, around 50 million tons of ethanol is produced this way and the volume is growing rapidly

[33]. Most of the ethanol is used as a gasoline additive, and is thus not really a value added chemical *per se*. However, considering the size of the ethanol production, one might consider using ethanol as a feedstock for chemical production. Since ethanol is a highly thermally stable and vaporizable feedstock compared to carbohydrates, gas-phase as well as liquid phase processes are possible. Oxidation of ethanol can lead to acetaldehyde, acetic acid or ethyl acetate, depending on the reaction conditions. The perhaps most interesting target is acetic acid, as this is produced on a multi-million tons scale and is mainly produced from the carbonylation of methanol today. Furthermore, acetic acid is probably the easiest accessible product from the oxidation of ethanol, apart from carbon dioxide. Recently, it was demonstrated that bio-ethanol can be oxidized with a 90% yield to acetic acid by using gold-nanoparticles and air at 150 ºC [34]. Dehydration of ethanol leads to ethylene. Ethylene is perhaps the most important chemical that is produced from petroleum, with an annual production exceeding 100M tons. Since dehydration of 100 kg of ethanol will only give 60 kg of ethylene at best, it is obvious that dehydration of ethanol can only meet a fraction of the ethylene demand. However, in recent years ethanol has been demonstrated to be a useful feedstock for the production of ethylene [35]. Thus, by the use of a solid acid catalyst, ethanol can be dehydrated in the gas phase at a moderate temperature of 140-250 ºC. Depending of the reaction conditions, ethanol can be dehydrated to form either diethyl ether or ethylene. It is also possible to use ethanol as a feedstock for the production of butadiene in the Lebedev process [36]. Although this process might seem a bit obscure, it has actually been used during the Second World War for the production of butadiene from grain ethanol in the USSR. The catalyst used is typically an oxide of aluminum or calcium and the reaction pathway involves reduction of ethanol to form acetaldehyde and aldol condensation of two molecules of acetaldehyde to form the C4 chain. Reduction and double dehydration leads to butadiene. Typically rather low yields of butadiene are obtained and this route is not at all competitive with the production of butadiene from oil and natural gas.

Ethanol is not the only product that can be obtained by fermentation of biomass. Some of the most interesting large scale chemicals that are made in this way are 1,3-propanediol, lactic acid and 3-hydroxy propionic acid, which can be dehydrated to acrylic acid [37]. All these chemicals are used for the production of polymers. Fermentation of glucose to 1,3-propanediol has recently been commercialized by DuPont and is used for the production of their so called “Sorona” fibers when polymerized with *tere*-phthalic acid [38]. Fermentation of glucose to lactic acid has been

commercialized by NatureWorks LLC. At full capacity, NatureWorks' plant in Nebraska will produce about 150.000 tons of lactic acid and utilize about 0.1% of the American corn production [39]. Lactic acid can be polymerized to form poly(lactic acid) (PLA) which has been found to possess many desirable properties as a thermoplastic. Furthermore, PLA is fully biodegradable and thus has a smaller environmental impact than traditional petroleum derived plastics. Finally, 3-hydroxy propionic acid can be produced by fermentation of glucose which after dehydration affords acrylic acid. Novozymes and Cargill have recently undertaken a joint venture to commercialize the production of acrylic acid via this combined fermentation-dehydration route [40].

2.2.2 Carbohydrates – gasification and pyrolysis

This approach is probably the least pretty and delicate one from a chemical point of view. Here carbohydrates are converted to syn-gas in a gasification reaction or to bio-oil using flash pyrolysis. Syn-gas can be used to produce a range of useful chemicals and fuels via traditional routes. Bio-oil is made by heating biomass to around 500-600 ºC in the absence of air for a few seconds [41]. This results in a rapid thermal decomposition to form a mixture of different products such as tar, phenolics, carboxylic acids, aldehydes and ketones. The product distribution is highly dependent on the exact pyrolysis conditions as well as the type of biomass used as feedstock. This oil could become a source of some valuable chemical building blocks. The overall advantage of this break-down-and-build-up approach is that the technology needed is relatively simple and cellulosic biomass and even lignin can be used as feedstock, rather than edible starch.

2.3 Glycerol

Glycerol is an important chemical by itself, as it is used widely as an additive in food and in cosmetics and many other places. However the massive amounts of glycerol that has flooded the market has led to a situation where the supply greatly exceeds the demand. This event has caused conventional glycerol production facilities to shut down. However, it has also led chemists to search for new processes which utilize glycerol as a feedstock for the production of value added chemicals [18, 42]. Some of the most important products that can be obtained from glycerol are shown in figure 2.3.

2.3.1 Glycerol – conventional chemical approach

Glycerol is, like carbohydrates, a highly functionalized molecule. However, unlike carbohydrates glycerol can be vaporized and reactions can be performed both in gas and liquid phase. Removal of functionality can be achieved by dehydration to afford two different products, depending on the catalyst and the reaction conditions. Dehydration over an acidic zeolite in the gas phase at 300 ºC has been demonstrated to yield primarily acrolein. The product selectivity is highly dependant on the exact acidity of the zeolite and yield of acrolein up to 73% has been reported [43]. Distillative

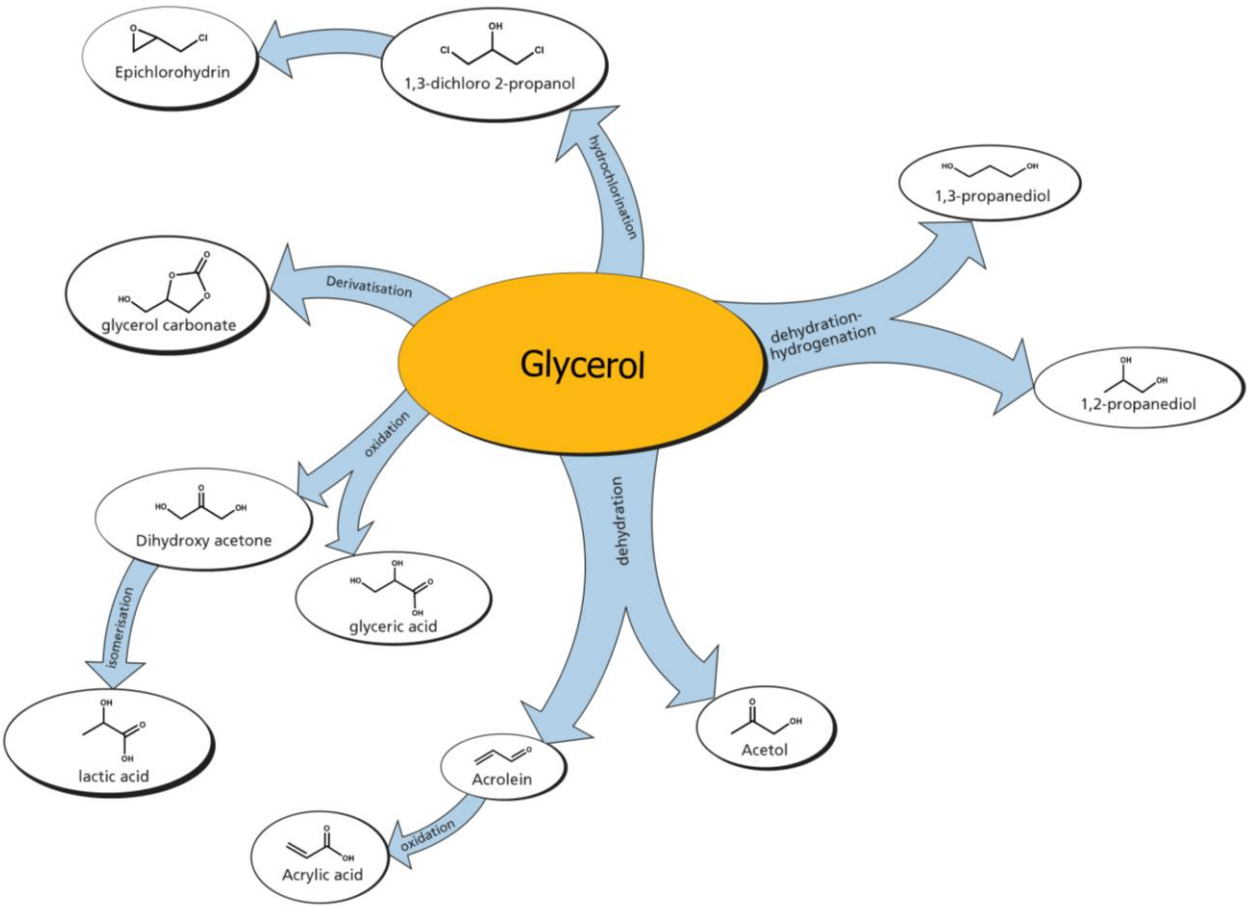


Figure 2.3 shows some of the most important and most studied examples of chemicals that can be produced from glycerol, either directly or indirectly.

dehydration over a copper-chromite catalyst has been demonstrated to give high yields of hydroxy acetone [44]. When the reaction is performed in a hydrogen atmosphere, reduction of hydroxy acetone leads to the formation 1,2-propane diol, which has been proposed as a substitute for the more toxic ethylene glycol in anti frost applications [18]. Aerobic oxidation of glycerol has been studied widely, and one of the most interesting procedures involves oxidation of a basic aqueous

solution of glycerol to give sodium glycerate by the use of a gold nanoparticle supported catalyst [45-46]. Sodium glycerate and glyceric acid are used as food additives to control pH. Oxidation of glycerol has also been achieved under acidic conditions using a carbon supported platinum-bismuth catalyst to afford mainly dihydroxyacetone [47, 48]. Another related example is the gold catalyzed oxidation of acrolein in methanol to give methyl acrylate in high yields [49]. This procedure in combination with the above-mentioned dehydration reaction would thus enable the overall conversion of glycerol to methyl acrylate.

2.3.2 Glycerol – fermentation

Selective oxidation of glycerol to glyceraldehyde has been achieved using the *gluconobactor suboxidans* strain [50]. However, more interesting is perhaps the fermentation of glycerol to 1,3-propanediol [51], although it seems unlikely that this route can compete with the fermentation of glucose to 1,3-propanediol.

2.3.3 Glycerol – catalytic reforming

Generation of hydrogen from biomass is a source of major interest since hydrogen is currently generated from fossil sources. Catalytic reforming of aqueous glycerol using a supported platinum catalyst has been demonstrated to give a 75% yield of hydrogen [52]. This procedure is also applicable to glucose although lower yields of hydrogen are achieved due to competing side-reactions. A less expensive Raney-NiSn catalyst has also been developed for this process, which gives comparable yields to the expensive platinum catalyst [53].

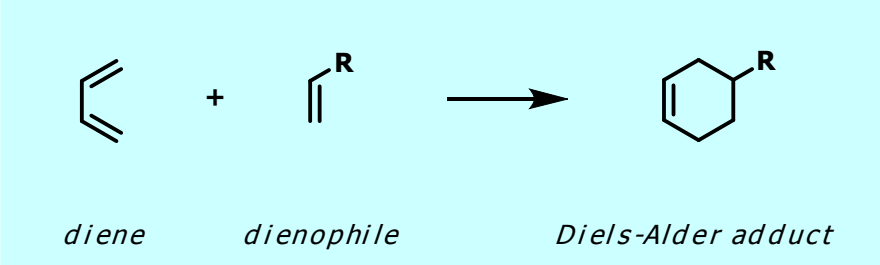
2.4 Outlook for the renewable chemical industry

It seems apparent that the chemical industry will have to adapt to a new source of raw materials instead of petroleum for the production of chemicals during the 21st century. However, this transition is likely to be very gradual, and take place only as new processes becomes economically viable alternatives. In the medium-range term, coal and gas are likely to play an important role in substituting petroleum, but in the long run, biomass is the only sustainable resource since it is annually renewable. As resources tend to become more expensive, recycling is also likely to become a significant source of building blocks for the chemical industry, and the “cradle-to-cradle” recycling capability of a particular product will be an important factor to weigh in when comparing different types of products.

Chemical ingenuity is the key element in developing new and efficient processes that utilize biomass as the feedstock. There are many possible approaches but in the end only the most economically attractive ones are likely to succeed. It is therefore possible that the future chemical industry will employ a much more diverse range of conversion tools rather than the current "homogeneous" chemical industry relying mainly on heterogeneous catalysis.

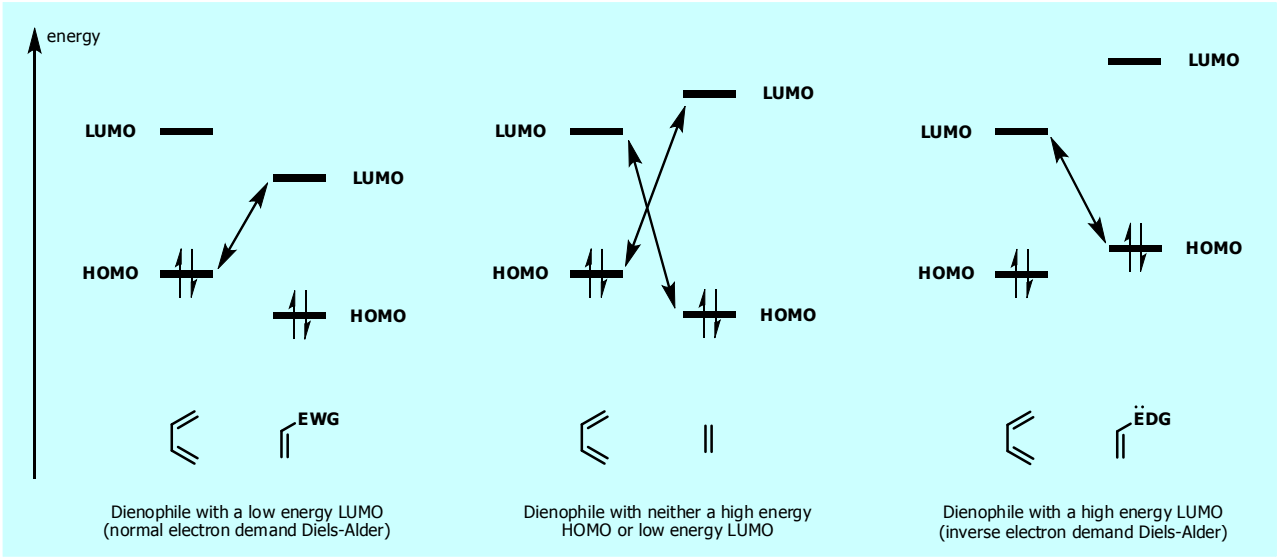
3. Aldehydes as Olefin Synthons in the Diels-Alder Reaction

The construction of complex organic molecules is an important discipline in many areas of chemistry. A prerequisite for total synthesis is the availability of a vast array of chemical transformations needed to synthesize the carbon skeleton, carry out the needed functionalizations and set the correct stereocenters. One of the most important tools for constructing 6-membered carbocycles is the Diels-Alder reaction [54-56]. The Diels-Alder reaction is an electrocyclization reaction between a 1,3-diene and a dienophile (scheme 3.1). The strength of the Diels-Alder reaction lies partly in the predictability of the stereochemical and regiochemical outcome and partly in the diversity of the reaction as numerous substrates can be used and many different variants of the reaction are known.



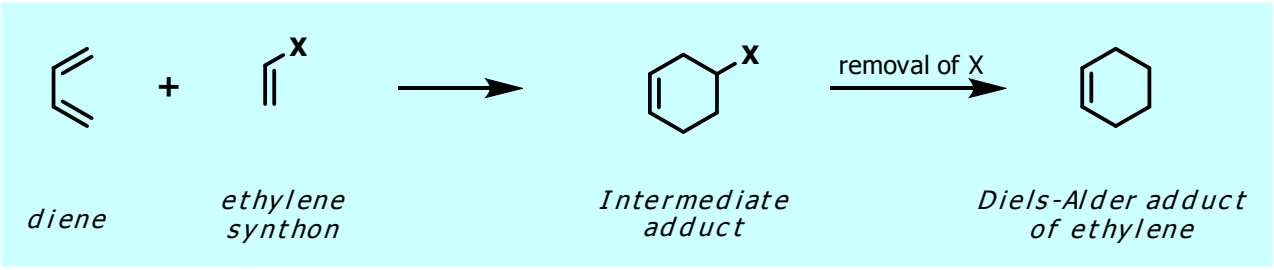
Scheme 3.1

The Diels-Alder reaction also has its disadvantages, though, as typically only substrates with electron withdrawing groups or electron donating groups undergo facile electrocyclization. This can be explained easily by looking at the relative energies of the frontier orbitals for the diene and the dienophile (scheme 3.2). In the normal electron demand Diels-Alder reaction, the HOMO (Highest Occupied Molecular Orbital) of the diene interacts with the LUMO (Lowest Unoccupied Molecular Orbital) of the dienophile, whereas it for the inverse electron demand Diels-Alder reaction is vice versa. The activation energy of a particular Diels-Alder reaction is equal to the energy difference between the HOMO-LUMO pairs of the diene-dienophile when neglecting other factors such as steric interactions. For simple olefins such as ethylene, the energy difference and thus the activation energy is very high, due to its high LUMO and low HOMO energy. For dienophiles with electron withdrawing substituents (EWG), the lower energy of the LUMO results in a lower energy difference and thus a lower activation energy. If the dienophile has an electron donating substituent (EDG) its HOMO energy is raised, resulting in a decrease in the energy difference between the dienophile HOMO and the diene LUMO and thus also results in an increased rate of the reaction.



Scheme 3.2

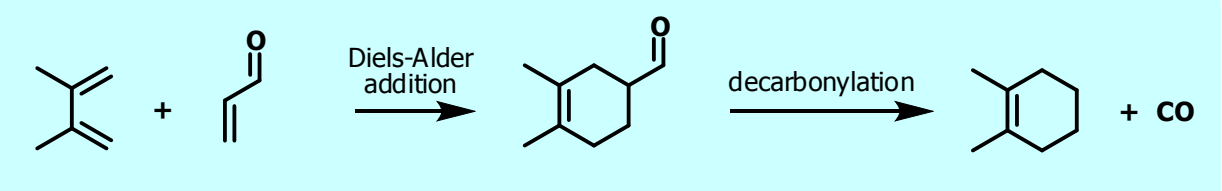
In order to carry out a selective Diels-Alder reaction with unreactive dienophiles such as ethylene or other simple olefins, synthons have to be used rather than the olefins themselves. The olefin synthons typically have a strongly electron withdrawing group attached that acts as a removable "handle", which after the electrocyclization reaction has taken place is removed using an appropriate reagent (scheme 3.3).



Scheme 3.3

From the perspective of green chemistry, the Diels-Alder reaction is a highly attractive reaction since 100% atom efficiency is achieved. However the use of olefin synthons changes this picture tremendously as pre-synthesis of the synthons is typically required. Furthermore removal of the electron withdrawing group of the synthon will necessarily lower the overall atom efficiency, not to mention the excessive amounts of reagents that typically must be used to remove the electron withdrawing groups. For the purpose of finding a more green and atom efficient Diels-Alder

version employing ethylene and olefin synthons, we envisioned the use of α,β-unsaturated aldehydes for the Diels-Alder reaction followed by removal of the aldehyde moiety using a decarbonylation catalyst (scheme 3.4).



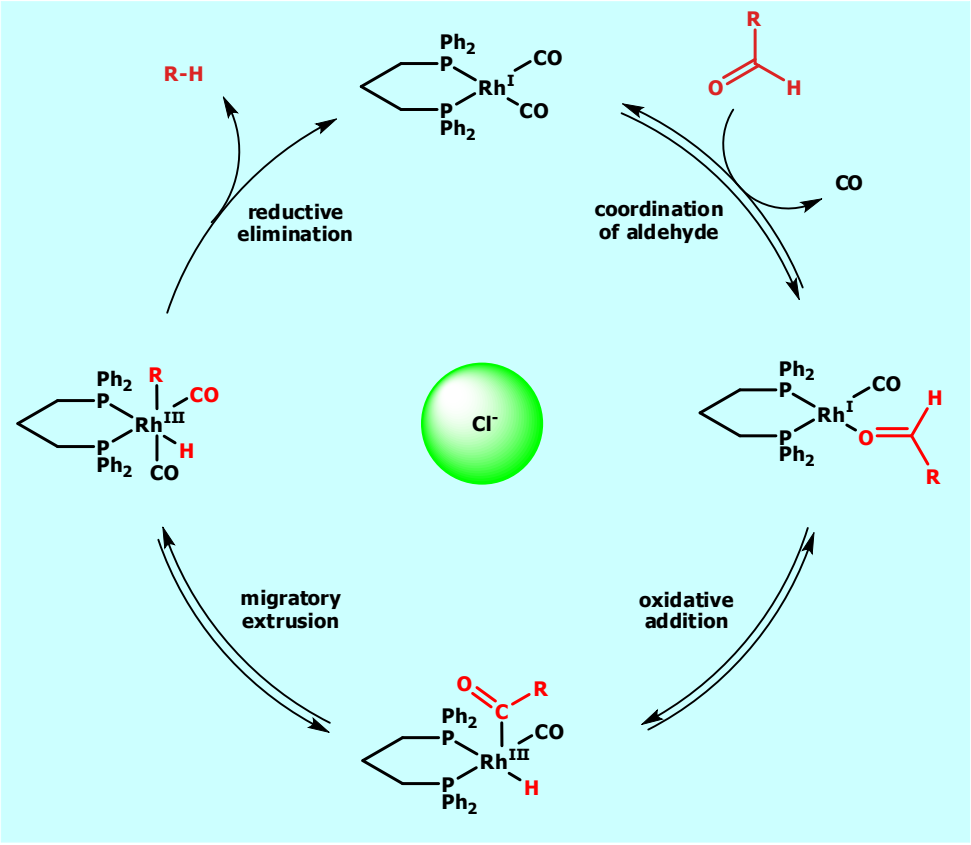
Scheme 3.4

This approach has some inherent advantages compared to existing methodology, namely that α,β-unsaturated aldehydes are readily available, CO is a relatively small handle that does not lower the atom efficiency significantly upon removal. Finally, removal of CO can be achieved using a decarbonylation catalyst rather than using a stoichiometric amount of a reagent that creates large amounts of waste. The remaining part of this chapter describes the development of a one-pot Diels-Alder decarbonylation reaction sequence and its implementation in the construction of various six-membered carbocycles.

3.1 Background on the rhodium catalyzed decarbonylation reaction

The rhodium mediated decarbonylation of aldehydes was first reported by Tsuji and Ohno in 1965 using Wilkinson's complex [57]. The decarbonylation reaction takes place at very mild conditions (20-110 ºC), but under these conditions Wilkinson's complex does not act as a catalyst, but is instead to be considered as a reagent, since loss of CO from $Rh(Cl)(CO)PPh_2$ does not occur under these conditions. If the temperature is raised to 210-230 ºC, the rhodium complex does act as a catalyst since loss of CO starts to take place and a catalytic decarbonylation cycle can occur [58]. In 1978 Doughty and Pignolet, in an effort to find a more efficient decarbonylation catalyst, studied the use of bi-dentate phosphine ligands instead of the previously examined mono-dentate ligands. Their approach was based on the assumption that a more cationic rhodium center, generated when two bi-dentate ligands coordinates to rhodium, does not bind as strongly to CO and hence will lose CO at lower temperatures. Their approach proved to be a success, as they discovered that complexes such as $Rh(dppp)_2Cl$ are capable of catalyzing aldehyde decarbonylation at temperatures of 115-180 ºC [59].

The rhodium catalyzed decarbonylation reaction has been subject to extensive studies in the Madsen group, with the primary goal of finding more and better ways to apply the reaction in organic synthesis. This has resulted in the discovery of *in situ* generation of $Rh(dppp)_2Cl$ from commercially available $RhCl_3 \cdot 3H_2O$ and dppp [60]. Using this method, many aldehydes can be decarbonylated in a very simple fashion and pre-synthesis of $Rh(dppp)_2Cl$ is therefore not required. It was furthermore discovered that the solvent plays an important role in the decarbonylation reaction. The most efficient solvent tested was diglyme (diethylene glycol dimethyl ether, bp. 162 ^oC), which is a water miscible polyether that is also capable of dissolving hydrocarbons. Another application that has been developed is the decarbonylation of non-protected aldoses [61]. Using this methodology, simple aldoses are decarbonylated to form the corresponding alditols. A mechanistic study of the rhodium catalyzed decarbonylation reaction has also been undertaken [62]. Here the mechanism was elucidated using both a DTF approach and an experimental Hammett study. The Hammett plots obtained had positive slopes, indicating that a negative charge is built up in the rate determining step. Relative energy comparisons indicates that a likely active catalytic specie is $[Rh(dppp)(CO)_2]^+$. The decarbonylation cycle consists of four overall steps (scheme 3.5).

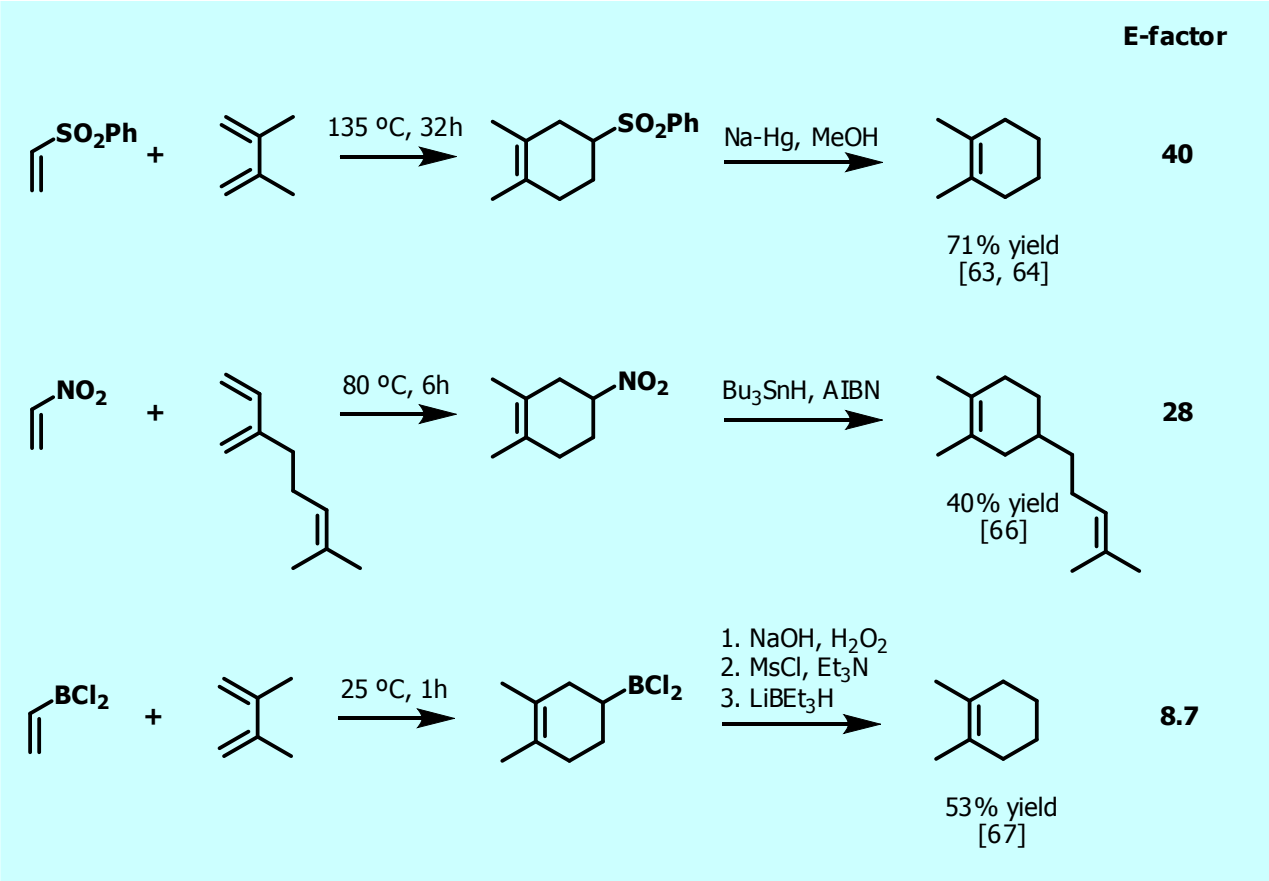


Scheme 3.5

The first step involves replacement of a carbonyl ligand with the aldehyde. Second step is oxidative addition to form a five coordinated acyl-hydride complex. The third and rate-determining step is migratory extrusion of carbon monoxide from the acyl moiety and the final step is reductive elimination to release the product paraffin and the catalyst that is ready for another cycle.

3.2 Background on the use of ethylene synthons in the Diels-Alder reaction

Several examples of ethylene synthons for the Diels-Alder reaction have been reported (scheme 3.6). Paquette reported in 1980 the use of phenyl vinyl sulfone as an ethylene synthon [63, 64]. Electrocyclization of phenyl vinyl sulfone and simple 1,4-dienes is facilitated by heating an excess of the 1,4-diene with phenyl vinyl sulfone at temperatures in the range of 25-155 ºC, depending on the reactivity of the diene. Subsequent workup of the addition products and removal of the sulfone moiety is achieved using sodium amalgam to furnish the desired Diels-Alder adduct of ethylene and the diene. This methodology has been employed in the total synthesis of different carbocycles [65].



Scheme 3.6

Another example of an ethylene synthon is nitroethene which undergoes a Diels-Alder reaction at moderate temperatures to form a secondary nitro-adduct [66]. The nitro-moiety is then removed using an excess of tributyl tin hydride. Dichloroborylethene has also been used and it is a highly reactive dienophile that undergoes cycloaddition reaction at room temperature. Removal of the dichloroboryl moiety is achieved by oxidative hydrolysis to form the corresponding alcohol followed by mesylation and reductive removal of the mesyl group [67]. An overview of the E-factors from the different methods is also given in scheme 3.6. The E-factors are calculated on basis of the experimental data given in the original reports [63, 64, 66, 67], and does not take solvents and simple inorganic salts such as NaCl and NaOH into consideration. Nor is any waste formed in the pre-synthesis of the ethylene synthons included in the calculation of the E-factors.

3.3 Results and discussion

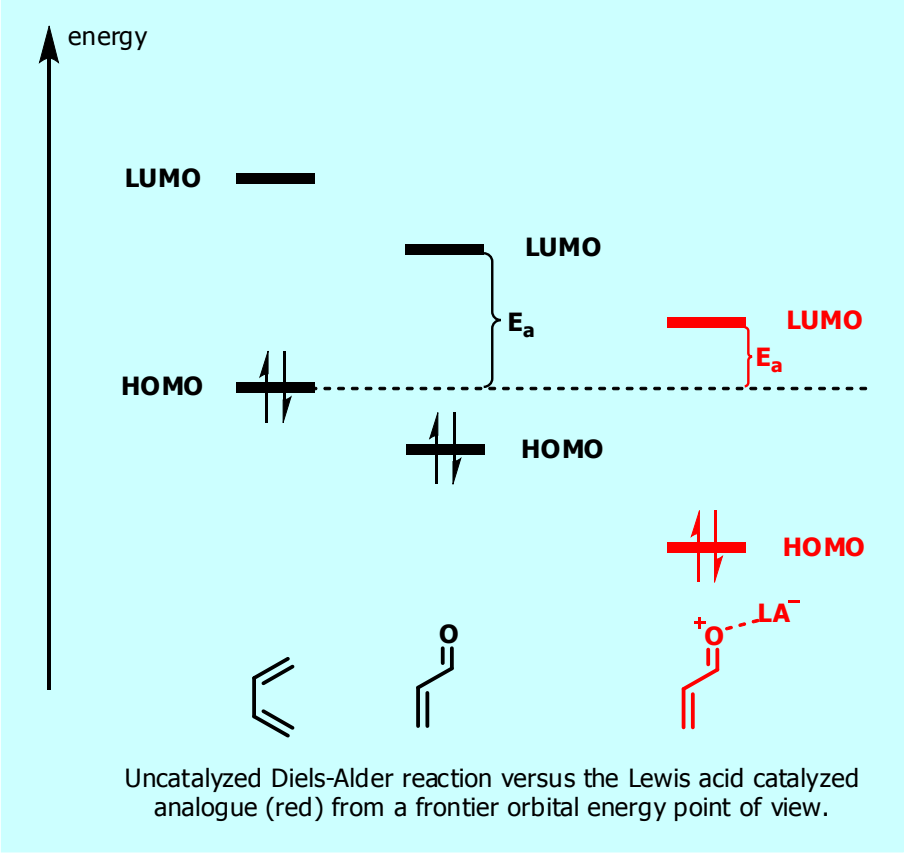
When designing a useful method for carrying out a Diels-Alder decarbonylation sequence, several factors have to be taken into account and several choices must be made. Simplicity of the method has to be weighed against overall method efficiency and in the end a compromise between the two must be reached. In this particular case, the choices that had to be made were mainly related to the execution of the Diels-Alder reaction, and the combination of the Diels-Alder reaction and the decarbonylation reaction.

3.3.1 Thermal Diels-Alder vs. Lewis acid catalyzed Diels-Alder

In general, the more electron withdrawing the substituent on the vinyl moiety is, the more reactive it will be in the Diels-Alder reaction. Acrolein is the simplest α,β-unsaturated aldehyde, and it can be viewed as simply being ethylene with a formyl group attached. The formyl group itself asserts a strong electron withdrawing effect on the C-C double bond, which, in combination with the fact that acrolein does not have any hindering substituents in the β-position, is responsible for the reactive nature of acrolein. Acrolein will react with most simple 1,4-dienes such as isoprene and 2,3-dimethyl butadiene at room temperature to give trace amounts of Diels-Alder adducts. However, in order to achieve full conversion within a reasonable time-frame, temperatures in excess of 100 ºC are required and for other, less reactive dienes, much higher temperatures are needed [68].

Acrolein has a boiling point of 53 ºC and it is therefore not possible to achieve a higher reaction temperature than this when working in an open reaction system. The easy solution is of course to

perform the cycloaddition reaction at elevated temperatures in an autoclave. However, although this approach might have proven successful for the use of reactive dienes and acrolein, less reactive dienes and other α,β-unsaturated aldehydes such as croton aldehyde would be reluctant to undergo a thermal electrocyclization reaction even at high temperatures. Furthermore, we learned that the decarbonylation reaction does not work well in a closed reaction system. Thus when acrolein and isoprene are heated to 170 °C for 24 hours in an autoclave in the presence of 2 mol% of $Rh(dppp)_2Cl$, the reaction mixture was found to contain 66% of the desired 1-methylcyclohexene and 34% of the Diels-Alder adduct which had not undergone decarbonylation. By comparison, decarbonylation of the same cycloaddition aldehyde could be achieved in an open flask at 170 °C. Here, full conversion was accomplished after just 4 hours. Evidently, the released CO in the autoclave is capable of hampering the decarbonylation cycle. Based on these observations and considerations we decided to pursue a Diels-Alder decarbonylation sequence based on an open system. It is noteworthy to mention that it was necessary to use preformed $Rh(dppp)_2Cl$ in this experiment since acrolein undergoes a spontaneous polymerisation reaction in presence of tertiary phosphines.

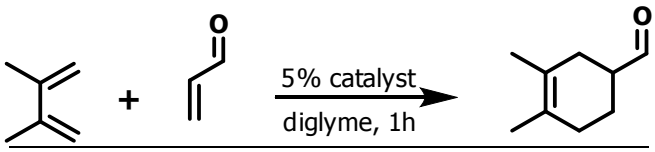


Uncatalyzed Diels-Alder reaction versus the Lewis acid catalyzed analogue (red) from a frontier orbital energy point of view.

Scheme 3.7

A remarkable feature of the Diels-Alder reaction is that it in many cases is subject to Lewis acid catalysis. Simply put, a Lewis acid coordinating to *e.g.* the formyl moiety of acrolein will enhance the electron withdrawing capability and make the vinyl moiety even more reactive. This can be visualized by the use of frontier orbital energies (scheme 3.7). This lowering of the LUMO energy can be very significant, and DFT-calculations of the Diels-Alder reaction between acrolein and isoprene have shown that if acrolein coordinates to aluminum chloride, a 47 Kcal/mol lowering of the activation energy is achieved [69]. This means that a cycloaddition reaction that would otherwise take place at elevated temperatures can take place at room temperature using an appropriate Lewis acid catalyst.

In order to find an optimal Lewis acid catalyst that is capable of catalyzing the Diels-Alder reaction at room temperature, a series of Lewis acids were screened using diglyme as solvent. The standard reaction used for the screening was the addition of acrolein to 2,3-dimethyl butadiene at room temperature (table 3.1).



Entry	Catalyst	Conversion of diene (%)[a]
1	$ZnCl_2$	<1
2[b]	$ZnCl_2$	>99
3	$AlCl_3$	43
4[c]	$BF_3 \cdot OEt_2$	>99
5[d]	$FeCl_3$	37
6	$La(OTf)_3$	<1
7	$Sc(OTf)_3$	66
8	$Bi(OTf)_3$	75
9	$RhCl_3 \cdot 3H_2O$	<1

Table 3.1. To a solution of 2,3-dimethyl-1,3-butadiene (5 mmol) and acrolein (7.5 mmol) in diglyme (5 mL) was added the Lewis acid (0.25 mmol) and the mixture was stirred at room temperature for 60 min. [a] Determined by GC. [b] Under neat condtions for 40 min. [c] Reaction time 10 min with 89% isolated yield of 3,4-dimethyl-3-cyclohexene-1-carbaldehyde. [d] Some by-products are visible by GC analysis.

Boron trifluoride diethyl etherate was found to be a far superior Lewis acid compared to standard metal chlorides and metal triflates. Although zinc chloride is capable of catalyzing the reaction under neat conditions to give very high yields of the cycloaddition product, it was not possible to use this in combination with the decarbonylation reaction, as the elevated temperatures required for the decarbonylation reaction turns zinc chloride into a powerful Lewis acid that will isomerize the double bond of the product and lead to an overall loss in product yield. It was not possible to quench the zinc chloride by addition of water or a base such as ethylene diamine. Under neat conditions, $AlCl_3$ and $BF_3{\cdot}OEt_2$, in comparison, led to complete decomposition of the starting materials. However when diglyme is used as solvent a smooth Diels-Alder reaction was achieved using $BF_3{\cdot}OEt_2$. Furthermore, quenching of BF_3 was achieved using a small amount of water and one equivalent of K_2HPO_4 relative to $BF_3{\cdot}OEt_2$. Other inorganic bases such as Na_2CO_3 or K_2CO_3 caused the decarbonylation reaction to give rise to side products and precipitation of rhodium metal.

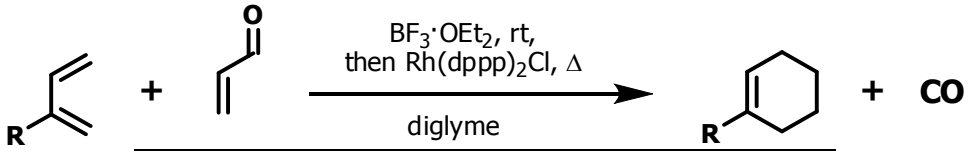
3.3.2 Decarbonylation of Diels-Alder adducts

As mentioned previously, a method for the *in situ* generation of the decarbonylation catalyst was developed by our group [60]. In this simple procedure, one equivalent of $RhCl_3{\cdot}3H_2O$ and two equivalents of dppp are mixed with the aldehyde in a diglyme solution. Heating this mixture to reflux temperature under argon atmosphere will furnish decarbonylation of the aldehyde. Disappointingly this method is not applicable to the selective decarbonylation of Diels-Alder aldehyde adducts, since double bond migration in the product olefin is taking place and lowers the yield of the reaction. This side reaction could be catalyzed by unreduced $RhCl_3{\cdot}3H_2O$ that is acting as a Lewis acid in a similar manner as $ZnCl_2$.

$Rh(dppp)_2Cl$ can be synthesized by reacting $RhCl_3{\cdot}3H_2O$ with COE in a reducing solvent (ethanol or isopropyl alcohol) followed by ligand exchange of the formed $[Rh(COE)_2Cl]_2$ with dppp [70]. For this work, a different method was chosen though. Refluxing one equivalent of $RhCl_3{\cdot}3H_2O$ with two equivalents of dppp in ethanol for 30 minutes under argon, followed by removal of the ethanol *in vacuo* afforded a crude catalyst that is equal in reactivity to the preformed $Rh(dppp)_2Cl$ made by ligand exchange. This catalyst did not form side products when it was used for decarbonylating Diels-Alder aldehyde adducts and it was therefore used for the final experimental procedure. The decarbonylation reactions were conveniently monitored by measuring the volume of gas (CO) that evolves using a displaceable water reservoir.

3.4 Scope and limitations for the use of acrolein as an ethylene synthon

The overall one-pot procedure involves reacting 1.5 equivalents of acrolein with 1 equivalent of the 1,4-diene in a diglyme solution in the presence of 6-10% $BF_3 \cdot OEt_2$ at room temperature. The Diels-Alder reaction takes from 10 to 300 minutes, depending on how reactive the particular diene is. Subsequent quenching of BF_3 using K_2HPO_4 and a small amount of water followed by addition of



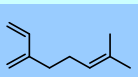
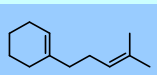
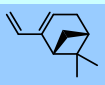
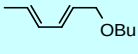
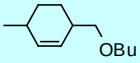
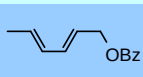
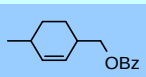
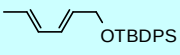
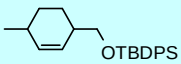
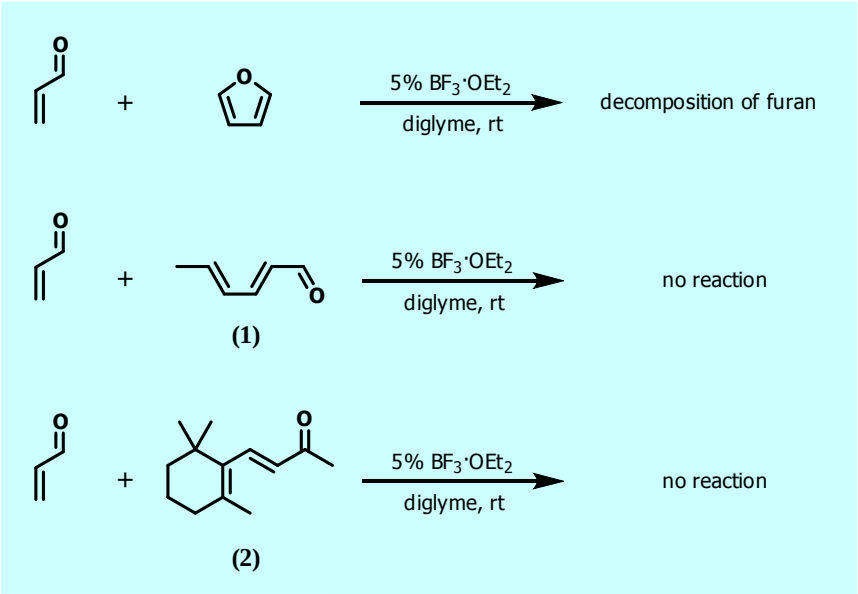
Entry	Diene	Product	Yield[a]
1			86%
2			65%
3			77%
4			75%
5			81%
6	 Ph	 Ph	84%
7[c]	 OBu	 OBu	79%
8	 OBu	 OBu	66%
9[b]	 OBz	 OBz	53%
10[c]	 OTBDPS	 OTBDPS	61%

Table 3.2. Acrolein as ethylene synthon in the Diels-Alder reaction. Reactions were carried out on a 5 – 40 mmol scale with 6 – 10% of $BF_3 \cdot OEt_2$ for the Diels-Alder reaction (10 – 300 min) and 0.3% of $Rh(dppp)_2Cl$ for the decarbonylation (8 – 20 hours). [a] Isolated yield. [b] Decarbonylation took 42 hours. [c] 1% of $Rh(dppp)_2Cl$ was used.

0.3-1% of $Rh(dppp)_2Cl$ and heating to reflux (162 ºC) until CO evolution has ceased affords the decarbonylated product. The decarbonylation reaction typically takes 8 to 20 hours. Work-up of the products is achieved by addition of water and extraction with pentane. Final purification is achieved by either distillation or column chromatography. In order to examine the scope and limitations, this procedure was tested on a series of dienes (table 3.2).

The Diels-Alder decarbonylation sequence works very well for simple hydrocarbon dienes where isolated yields around 80% are typically obtained (entry 1-6). Most of these products are highly volatile and a product loss during work-up is probably unavoidable in some cases (entry 2). Dienes containing ether and ester functionalities are also within the scope of this procedure, although slightly lower yields are obtained than for the hydrocarbon dienes. The lower yield is likely related to the long reaction time needed for the Diels-Alder reaction to reach completion, since BF_3 causes a slow decomposition of the allyl ether and ester dienes according to TLC. Some dienes do not undergo the Diels-Alder reaction under these conditions. Furan was found to decompose in the presence of BF_3 and dienes containing electron withdrawing groups such as sorbic aldehyde (**1**) and β-ionone (**2**) do not react with acrolein under these conditions (scheme 3.8).



Scheme 3.8

The procedure seems to be applicable to many Lewis acid resistant dienes and gives yields that are comparable to, or higher than the existing ethylene synthon procedures mentioned previously. The E-factor for the conversion of 2,3-dimethyl butadiene to form 1,2-dimethylcyclohexene is just 1.1

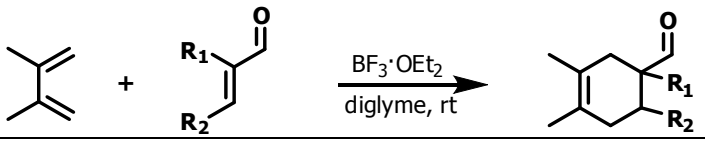
when calculated in the same way as for the other procedures reported (scheme 3.6), illustrating that this procedure does not result in the formation of large amounts of waste. Furthermore, this procedure can be performed in one pot, which is beneficial since most of the dienes will give rise to the formation of several possible Diels-Alder adducts. However after the decarbonylation stage, all these isomers are decarbonylated to form the same single cyclohexene product. If a particular diene is sensitive to Lewis acids, however, it could prove more advantageous to carry out the Diels-Alder reaction thermally, followed by a decarbonylation reaction in an open flask.

3.5 Propylene and styrene synthons

Further examination of the scope and limitations were aimed towards examining the use of other α,β-unsaturated aldehydes than acrolein. Here, crotonaldehyde and methacrolein can be envisioned as synthons for propylene and cinnamaldehyde as a synthon for styrene.

3.5.1 Diels-Alder reactivity for different α,β-unsaturated aldehydes

The reactivity of different α,β-unsaturated aldehydes in the Diels-Alder reaction with 2,3-dimethyl butadiene was initially examined. Interestingly, the same electrocyclization procedure that was applicable for acrolein is also applicable for other, less reactive dienophiles by simply increasing the catalytic amount of boron trifluoride and extending the reaction time (table 3.3).



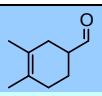
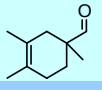
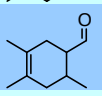
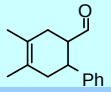
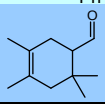
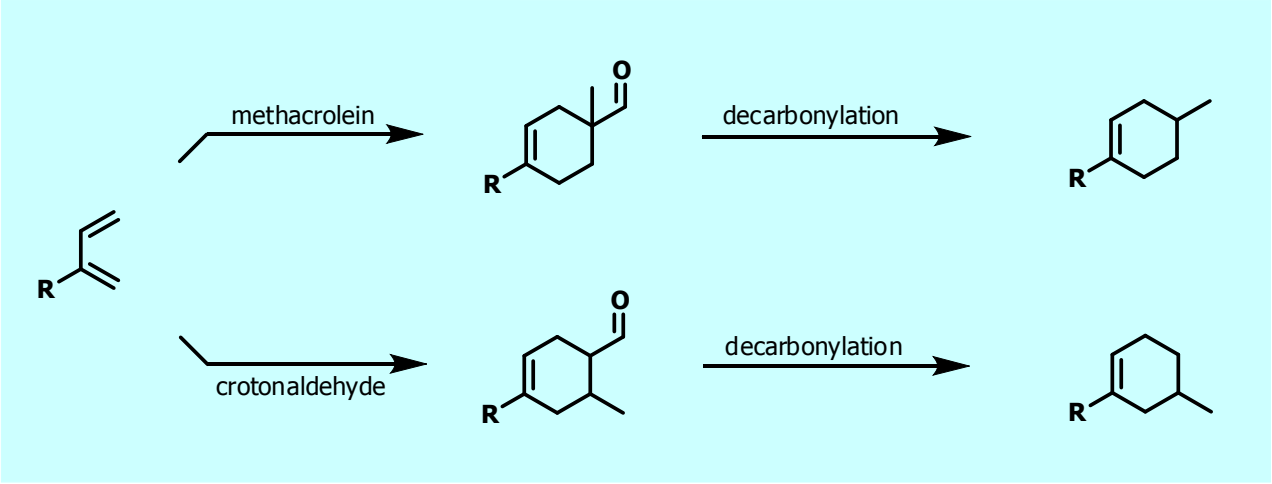
Entry	Dieno-phile	$BF_3 \cdot OEt_2$ loading	Reaction time	Product	Yield[a]
1[b]		5%	10 min		87%
2		10%	30 min		95%
3		10%	6 hours		89%
4		15%	24 hours		74%
5		30%	24 hours		trace

Table 3.3. Reactions were performed with 30 mmol of diene and 45 mmol of dienophile in 30 mL of diglyme. [a] Isolated yield. [b] Diethyl ether was used instead of diglyme.

Notably, methacrolein gives higher yields of the Diels-Alder adduct than even acrolein. This is possibly related to the α-tribranched cycloadduct being incapable of undergoing aldol-type self condensation. β-Substituted aldehydes such as crotonaldehyde and cinnamaldehyde are less reactive, but still give reasonable amounts of the Diels-Alder adduct. However the β,β-disubstituted aldehyde 3-methyl crotonaldehyde proved to be completely unreactive and gave only rise to the formation of trace amounts of the Diels-Alder adduct.

3.5.2 Decarbonylation of other Diels-Alder adducts

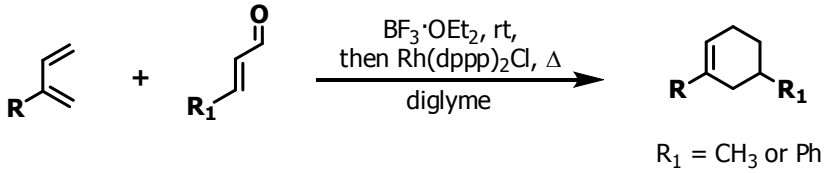
Since methacrolein and crotonaldehyde both undergo the Diels-Alder cycloaddition, two propylene synthons could be realized. The use of boron trifluoride as a Lewis acid has a very strong influence on the regioselectivity of the product formed when the diene is unsymmetrical. Thus, methacrolein and crotonaldehyde could be envisioned not just as propylene synthons but as complementary regioselective propylene synthons (scheme 3.9).



Scheme 3.9

It turned out, however, that the α-tribranched cycloadduct formed by cycloaddition between methacrolein and a diene does not undergo decarbonylation at the standard decarbonylation conditions used for the previous aldehydes. At increased temperatures (215 ºC) and in the absence of a solvent, it was possible to form small amounts of the decarbonylated product. However, this was accompanied by side products arising from the migration of the C-C double bond. It was thus obvious that methacrolein is not a useful propylene synthon since it does not undergo decarbonylation at moderate temperatures. This failure to undergo decarbonylation has been

reported previously for a similar hindered aldehyde [60]. Crotonaldehyde on the other hand was found to be a useful propylene synthon, as its Diels-Alder adduct undergoes decarbonylation at moderate conditions (162 ºC). Similarly, the method was applied successfully to cinnamaldehyde as a synthon for styrene (table 3.4).



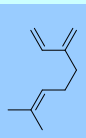
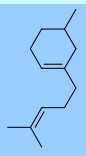
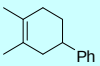
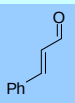
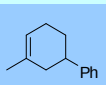
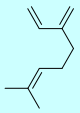
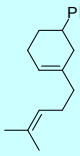
Entry	Diene	Dienophile	Major product	Regioisomer ratio	Yield[a]
1[b]				-	86%
2[b]				24:1	67%
3[b]				24:1	88%
4[c]				-	73%
5[c]				39:1	59%
6[c]				39:1	75%

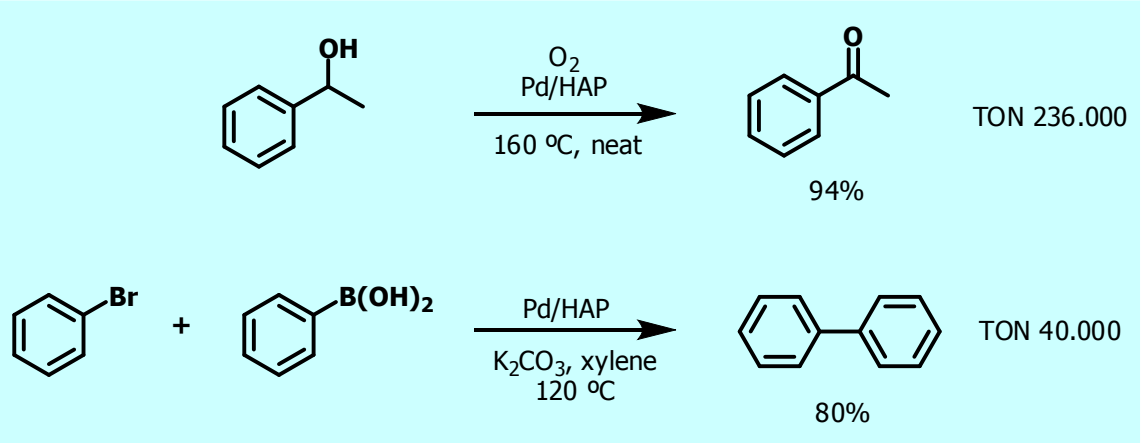
Table 3.4. Diels-Alder decarbonylation protocol with various α,β-unsaturated aldehydes. Reactions were carried out with 10 – 15% of $BF_3{\cdot}OEt_2$ for the Diels-Alder reaction and 0.3% of $Rh(dppp)_2Cl$ for the decarbonylation (14 – 30 hours). [a] Isolated yield of both isomers. [b] 10% of $BF_3{\cdot}OEt_2$ was used for 5-6 hours. [c] 15% of $BF_3{\cdot}OEt_2$ was used for 24 hours.

In general, comparable yields are obtained in the procedure as when using acrolein as ethylene synthon. The method thus appears to be generally applicable to dienophiles such as acrolein and α,β-unsaturated aldehydes that are mono-substituted in the β-position such as crotonaldehyde and

cinnamaldehyde. For the Diels-Alder decarbonylation reactions with crotonaldehyde and cinnamaldehyde two different regioisomeric olefins ("para" and "meta") were observed. The two regioisomers could not be separated and they were therefore quantified by GC-MS based on their relative intensities. Since the Diels-Alder reaction is subject to Lewis acid catalysis, excellent regioselectivity is achieved in both cases. This high regioselectivity underscores the potential of using the aldehyde moiety as a removable handle, not just to increase the reactivity of the dienophile, but also to steer a substituent into a desired position in the construction of a carbocycle.

3.6 Decarbonylation using palladium nanoparticles

During my stay in Japan, I had the chance to investigate a different class of decarbonylation catalysts, namely supported palladium nanoparticles. Supported palladium nanoparticles have been reported previously as being highly active cross-coupling and oxidation catalysts [71, 72] (scheme 3.10).



Scheme 3.10

When palladium is used as an oxidation catalyst, oxidation has been reported to be accompanied by small amounts of decomposition of the product aldehyde resulting from decarbonylation [73]. This indicates that palladium can be an active decarbonylation catalyst and thus led us to investigate supported palladium nanoparticles. Being heterogeneous in nature, this type of catalyst is markedly different than the homogeneous $Rh(dppp)_2Cl$ complex used so far. Palladium nanoparticles on different supports were prepared and compared for the decarbonylation of a Diels-Alder aldehyde adduct.

3.6.1 Preparation of the catalysts

Three different supports were used, namely TiO_2, hydrotalcite (HT) and hydroxyapatite (HAP). Hydrotalcite is a layered, mixed hydroxide of magnesium and aluminum that has cation and anion exchange capability as well as adsorption capacity. Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) which is a major component of human bone and teeth is a calcium phosphate mineral that also has ion exchange capability and adsorption capacity.

The palladium nanoparticle catalysts (1 wt%) are prepared by immobilization of a Pd(II) precursor on the support material. For HT the anionic palladium precursor, $Na_2[PdCl_4]$ was used. The cationic precurser $Pd(CF_3CO_2)_2$ was used for the TiO_2 and HAP supports. Reduction of the immobilized Pd(II) precursor was subsequently achieved using either KBH_4 or H_2 as the reductant.

3.6.2 Evaluation of the catalysts

The activity of the catalysts was evaluated for the decarbonylation of 2-napthaldehyde in refluxing xylene using an argon atmosphere. The appearance of naphthalene was followed by GC (figure 3.1). Interestingly, all of the palladium nanoparticle catalysts are active as decarbonylation catalysts. Pd/TiO_2 is superior to Pd/HT and Pd/HAP which both show equal activity. Heterogeneous catalysts are generally easy to separate from the reaction mixture and can often be reused many times. A reuse study was therefore also undertaken for the most active Pd/TiO_2 catalyst (figure 3.2).

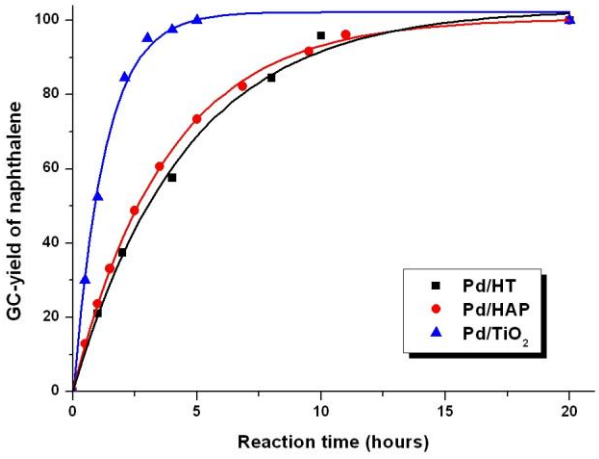


Figure 3.1. Decarbonylation of 2-naphthaldehyde using palladium catalysts (H_2-reduced) in refluxing xylene (140 °C). 1.0 mmol 2-naphthaldehyde, 100.0 mg catalyst (1 wt% Pd), 5.0 ml xylene, argon atmosphere.

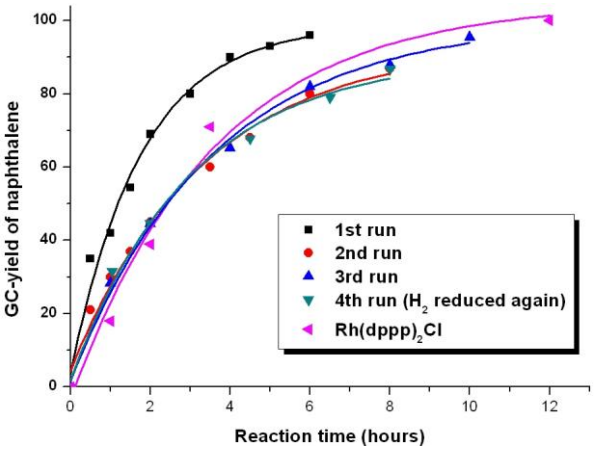
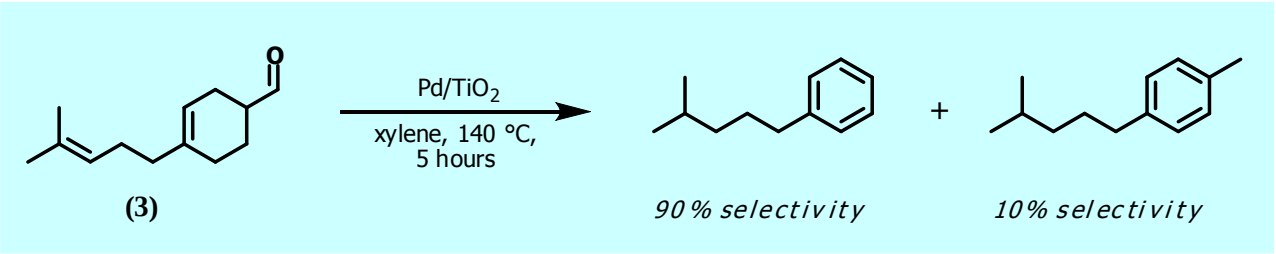


Figure 3.2. Reuse of the same batch of Pd/TiO_2 (1 wt% Pd, H_2-reduced, 0.0094 mmol Pd) and use of $Rh(dppp)_2Cl$ (0.01 mmol) in refluxing xylene (5.0 ml, 1.0 mmol 2-naphthaldehyde).

An activity loss is observed after the first run, after which the activity of the Pd/TiO_2 catalyst remains fairly constant. Fresh H_2-reduction of the used catalyst did not reactivate the catalyst to the activity level of the first run, however the catalyst retains an activity that is comparable to the homogeneous rhodium complex $Rh(dppp)_2Cl$. The same level of activity is obtained when using either KBH_4 or H_2 as the reducing agent. The palladium nanoparticle catalysts are sensitive to oxygen, though. This is illustrated by a comparison between experiments performed in argon and in oxygen atmosphere in refluxing mesitylene. Thus, after 1.5 hours, only 33% decarbonylation of naphthalene has taken place when bubbling oxygen through the reaction mixture for Pd/TiO_2, as opposed to 85% decarbonylation in an argon atmosphere.

3.6.3 Selectivity of the palladium nanoparticle catalyst

As the Pd/TiO_2 catalyst is comparable in activity for decarbonylation of 2-napthaldehyde as $Rh(dppp)_2Cl$, it was decided to evaluate its potential as a catalyst for the decarbonylation of more demanding substrates, such as **3** which is prone to double bond migration and dehydrogenation reactions. Unfortunately it turned out that the Pd/TiO_2 catalyst is completely unselective towards giving the desired decarbonylated product. Instead dehydrogenation to form aromatic products takes place in addition to decarbonylation (scheme 3.10).



Scheme 3.10

The supported palladium nanoparticle catalysts are therefore not useful for the decarbonylation of sensitive substrates which are prone to undergo dehydrogenation reactions. However in the case of aromatic aldehydes that are stable towards this type of side-reaction the palladium catalysts are interesting alternatives to homogeneous rhodium complexes due to their ease of reuse.

3.7 Summary

The decarbonylation reaction has been applied in combination with the Diels-Alder reaction in a one-pot reaction sequence that allows commercially available α,β-unsaturated aldehydes to be used as olefin synthons [74]. The reaction sequence is advantageous to existing methods since low amounts of waste are formed and the reaction features excellent regioselectivity for dienophiles such as crotonaldehyde and cinnamaldehyde. Further development in this area could be envisioned to be the use of enantioselective catalysts for the Diels-Alder reaction in combination with the decarbonylation reaction. This would allow *e.g.* crotonaldehyde to be used as an enantioselective propylene synthon.

Additionally, palladium nanoparticles were evaluated as decarbonylation catalysts and were found to display comparable activity to $Rh(dppp)_2Cl$ although they are at the same time much less selective for demanding substrates that are prone to double bond migration and dehydrogenation.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 instrument. Chemical shifts were correlated relative to chloroform (7.26 ppm and 77.00 ppm, respectively). The data were processed with MestReC 4.7.4.0 software. GC-MS analysis was performed on a Shimadzu Spectachrom QP5000 GC-MS with a Supelco Equity-1 column (30 m in length, an inner diameter of 0.25 mm, and an inner film of dimethyl polysiloxane). Optical rotation was measured on a Perkin-Elmer 241 Polarimeter.

Reactions were carried out using flame dried glassware and a protective argon atmosphere in all cases. Argon atmosphere was achieved with a manifold system by first evacuating the reaction flask and then allowing for an inflow of argon. This cycle was repeated 5 times. All chemicals were used as received, except where otherwise noted.

Silica gel 60 (220-440 mesh, Fluka) was used for column chromatography. The same silica was used for TLC (Silica gel 60 F_{254}, Merck). TLC's of aldehydes were processed by using 2,4-dinitro-phenylhydrazine and TLC's of olefins were processed by using $KMnO_4$.

DMF and diethyl ether were dried over 4Å molecular sieves. Diglyme was used as received (water content of up to 100 ppm is not detrimental to the Diels-Alder reaction, but a higher water concentration will hydrolyze boron trifluoride and significantly lower the reaction rate).

Acrolein, methacrolein and crotonaldehyde form low-boiling azeotropes with water and were therefore purified by two distillations, the final one over flame dried calcium sulfate (1:1 weight ratio). They were stored in a dark bottle over a small amount of hydroquinone (~0.1%). Furthermore, methacrolein and crotonaldehyde were stored at 5 °C. The aldehydes are stable for many months when stored in this way, and no special precautions are necessary when opening the flasks and taking out a sample. Cinnamaldehyde was vacuum distilled once and the same batch was used for many weeks.

All dienes were stored in a refrigerator. Isoprene, myrcene, 2-phenyl-1,3-butadiene and 2-(butoxymethyl)-1,3-butadiene are not stable for many weeks, and were thus distilled prior to use. Myrcene and (1*R*)-nopadiene contain some isomeric impurities that could not be separated (less than 10%). Some of these impurities remain in the final products, as they do not participate in the reaction. Based on GC-MS and NMR data, the percentage of impurities present was determined and subtracted to give the product yield.

High resolution mass spectrometry was carried out at the Department of Physics and Chemistry, University of Southern Denmark while microanalyses were conducted at the Institute of Physical Chemistry, University of Vienna.

General Procedure for Diels-Alder Decarbonylation Sequence: A solution of $RhCl_3 \cdot 3H_2O$ (29.3 mg, 0.111 mmol) and dppp (95.6 mg, 0.225 mmol) in ethanol (10 mL) was degassed and heated to reflux for 30 min. The mixture was then concentrated to afford crude $Rh(dppp)_2Cl$ as a yellow solid which was dissolved in diglyme (2 mL). Another flask was charged with diglyme (40 mL), diene (39 mmol) and aldehyde (60 mmol) followed by addition of $BF_3 \cdot OEt_2$ (0.30 – 0.74 mL, 2.4 – 5.9 mmol). The mixture was stirred at room temperature until the cycloaddition reaction had gone to completion according to GC or TLC. The mixture was quenched with $K_2HPO_4 \cdot 3H_2O$ (0.60 – 1.2 g, 2.4 – 5.9 mmol) and water (0.25 mL). The above catalyst solution was added and the reaction was degassed and heated to reflux until the decarbonylation had gone to completion. The mixture was cooled to room temperature (figure 3.3), diluted with water (50 mL) and extracted with pentane (5 × 50 mL). The combined organic phases were washed with water (5 × 50 mL) and dried with anhydrous Na_2SO_4. Pentane was removed by distillation followed by isolation of the product cyclohexene by either distillation or flash chromatography. The decarbonylation reaction could be monitored by measuring the evolution of carbon monoxide. This was achieved by connecting the reaction flask to a burette filled with water. The bottom of the burette was further connected to a reservoir flask with water. In this way, carbon monoxide from the reaction forces water from the burette into the reservoir flask.

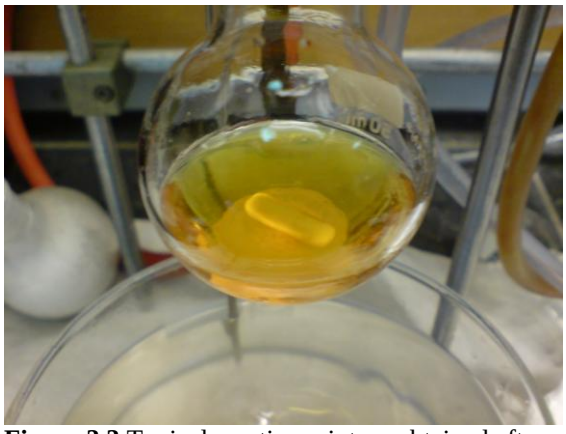


Figure 3.3 Typical reaction mixture obtained after the Diels-Alder decarbonylation reaction sequence.

1,2-Dimethylcyclohexene: b.p. 134-136 °C (lit. [67] b.p. 135-136 °C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.50-1.60 (m, 4H), 1.61 (s, 6H), 1.86-1.97 ppm (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.14, 23.46, 31.71, 125.60 ppm; MS: *m*/*z*: 110 $[M]^+$.

1-Methylcyclohexene: b.p. 107-110 °C (lit. [75] b.p. 106-110 °C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.49-1.67 (m, 4H), 1.64 (s, 3H), 1.87-2.01 (m, 4H), 5.36-5.42 ppm (tdd, 1H, *J* = 1.5 Hz, *J* = 3.4 Hz, *J* = 5.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.37, 22.99, 23.94, 25.28, 30.02, 121.10, 134.05 ppm; MS: *m*/*z*: 96 $[M]^+$.

1-(4-Methyl-3-pentenyl)cyclohexene: b.p. 100-102 °C at 17 mm Hg; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.48-1.66 (m, 4H), 1.60 (s, 3H), 1.68 (s, 3H), 1.88-2.12 (m, 8H), 5.06-5.15 (m, 1H), 5.37-5.42 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 17.65, 22.57, 23.02, 25.23, 25.69, 26.46, 28.37, 38.09, 120.66, 124.47, 131.23, 137.72 ppm; MS: *m*/*z*: 164 $[M]^+$. NMR data are in accordance with literature values [64].

Bicyclo[2,2,2]-2-octene: ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.10-1.19 (m, 4H), 1.36-1.46 (m, 4H), 2.35-2.43 (m, 2H), 6.12-6.19 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.75, 29.46, 134.21 ppm; MS: *m*/*z*: 108 $[M]^+$. NMR data are in accordance with literature data [67].

9,9-Dimethyltricyclo[4,4,0,1^{8,10}]-1-undecene: b.p. 115-120 °C at 15 mm Hg (lit. [67] b.p. 118-123 °C at 15 mm Hg); $[\alpha]_D^{20}$ = -29.9 (*c* = 2.2, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.84 (d, 1H, *J* = 9.3 Hz), 0.97 (s, 3H), 1.13-1.23 (m, 1H), 1.25 (s, 3H), 1.40-1.48 (m, 1H), 1.56-1.71 (m, 1H), 1.76-1.90 (m, 2H), 1.94-2.11 (m, 3H), 2.11-2.24 (m, 1H), 2.41 (t, 1H, *J* = 5.8 Hz), 2.45-2.61 (m, 2H), 5.14 ppm (q, 1H, *J* = 3.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.79, 23.57, 24.53, 27.19, 32.56, 33.37, 33.55, 35.59, 39.56, 42.17, 52.22, 116.88, 146.73 ppm; MS: *m*/*z*: 176 $[M]^+$.

1-Phenylcyclohexene: b.p. 122-125 °C at 13 mm Hg (lit. [76] b.p. 128 °C at 16 mm Hg); R_f = 0.45 (EtOAc/hexane, 1:99); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.63-1.73 (m, 2H), 1.75-1.84 (m, 2H), 2.18-2.27 (m, 2H), 2.39-2.47 (m, 2H), 5.13-5.19 (m, 1H), 7.19-7.42 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.40, 23.31, 26.12, 27.63, 125.00, 125.16, 126.73, 128.40, 136.80, 142.92 ppm; MS: *m*/*z*: 130 $[M - C_2H_4]^+$.

1-(Butoxymethyl)cyclohexene: b.p. 95-102 °C at 15 mm Hg; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.90 (t, 3H, *J* = 7.3 Hz), 1.30-1.43 (m, 2H), 1.49-1.68 (m, 6H), 1.93-2.05 (m, 4H), 3.35 (t, 2H, *J* = 6.6 Hz), 3.78-3.80 (m, 2H), 5.63-5.69 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.92, 19.39, 22.42, 22.52, 24.97, 25.86, 31.85, 69.62, 75.56, 124.47, 135.21 ppm; HRMS calcd for $C_{11}H_{20}ONa$: 191.1412 $[M + Na]^+$; found: 191.1403.

3-(Butoxymethyl)-6-methylcyclohexene: R_f = 0.67 (Et_2O/pentane, 1:19); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.87-0.97 (m, 6H), 1.21-1.45 (m, 3H), 1.48-1.72 (m, 5H), 2.09-2.39 (m, 2H), 3.19-3.31 (m, 2H), 3.36-3.46 (m, 2H), 5.52-5.66 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.94, 19.37, 21.43, 23.15, 27.95, 29.99, 31.81, 35.26, 70.81, 74.56, 127.25, 134.88 ppm; HRMS calcd for $C_{12}H_{22}ONa$: 205.1568 $[M + Na]^+$; found: 205.1563.

(4-Methyl-2-cyclohexenyl)methyl benzoate: R_f = 0.55 (EtOAc/heptane, 1:99); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.00 (d, 3H, *J* = 7.1 Hz), 1.30-1.45 (m, 1H), 1.56-1.79 (m, 3H), 2.15-2.27 (m, 1H), 2.50-2.61 (m, 1H), 4.20 (d, 1H, *J* = 1.3 Hz), 4.22 (s, 1H), 5.58-5.76 (m, 2H), 7.40-7.59 (m, 3H), 8.03-8.08 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ =

21.27, 23.03, 27.73, 29.82, 34.42, 67.90, 125.81, 128.29, 129.51, 130.36, 132.81, 135.95, 166.56 ppm; HRMS calcd for $C_{15}H_{18}O_2Na$: 253.1205 $[M + Na]^+$; found: 253.1206.

***tert*-Butyl((4-methyl-2-cyclohexenyl)methoxy)diphenylsilane**: R_f = 0.30 (EtOAc/heptane, 1:39); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.99 (d, 3H, *J* = 3.7 Hz), 1.11 (s, 9H), 1.22-1.34 (m, 1H), 1.63-1.75 (m, 3H), 2.13-2.42 (m, 2H), 3.50-3.65 (m, 2H), 5.57-5.70 (m, 2H), 7.37-7.49 (m, 6H), 7.70-7.76 ppm (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.30, 21.39, 22.72, 26.87, 27.97, 29.99, 37.74, 67.32, 127.28, 127.56, 129.48, 133.98, 134.89, 135.60; HRMS calcd for $C_{24}H_{32}OSiNa$: 387.2120 $[M + Na]^+$; found: 387.2120.

1,2,4-Trimethylcyclohexene: b.p. 150-154 °C (lit. [77] b.p. 154 °C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.94 (d, 3H, *J* = 2.6 Hz), 1.08-1.23 (m, 1H), 1.24-1.70 (m, 9H), 1.85-2.11 ppm (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 18.86, 19.10, 21.95, 29.32, 31.73, 31.98, 40.53, 125.14, 125.16 ppm; MS: *m*/*z*: 124 $[M]^+$.

1,5-Dimethylcyclohexene: b.p. 132-133 °C (lit. [78] b.p. 127-129 °C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.93-0.98 (m, 3H), 1.03-1.19 (m, 1H), 1.51-1.73 (m, 6H), 1.87-2.06 (m, 3H), 5.33-5.40 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.97, 23.74, 25.36, 28.89, 30.63, 38.73, 120.64, 133.65 ppm; MS: *m*/*z*: 110 $[M]^+$.

5-Methyl-1-(4-methyl-3-pentenyl)cyclohexene: b.p. 107-108 °C at 12 mm Hg; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.96 (d, 3H, *J* = 2.7 Hz), 1.05-1.22 (m, 1H), 1.54-1.75 (m, 9H), 1.87-2.13 (m, 7H), 5.06-5.16 (m, 1H), 5.35-5.41 ppm (s, br, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 17.67, 22.00, 25.33, 25.70, 26.49, 28.92, 30.83, 37.07, 37.91, 120.26, 124.47, 131.22, 137.29 ppm; MS: *m*/*z*: 178 $[M]^+$.

1,2-Dimethyl-4-phenylcyclohexene: b.p. 130-131 °C at 13 mm Hg (lit. [79] b.p. 128-130 °C at 11 mm Hg); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.65-1.70 (m, 6H), 1.71-2.29 (m, 6H), 2.73-2.86 (m, 1H), 7.18-7.38 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 18.87, 19.05, 30.29, 32.35, 40.05, 40.91, 125.32, 125.48, 125.85, 126.84, 128.28, 147.32 ppm; MS: *m*/*z*: 186 $[M]^+$.

1-Methyl-5-phenylcyclohexene: b.p. 122-123 °C at 13 mm Hg; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.58-1.74 (m, 1H), 1.68 (s, 3H), 1.83-1.93 (m, 1H), 2.01-2.20 (m, 4H), 2.78-2.90 (m, 1H), 5.42-5.49 (s, br, 1H), 7.14-7.33 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 23.62, 25.82, 29.45, 38.31, 40.54, 120.86, 125.91, 126.86, 128.32, 133.77, 147.30 ppm; MS: *m*/*z*: 172 $[M]^+$. ^{13}C NMR data are in accordance with literature data [80].

5-Phenyl-1-(4-methyl-3-pentenyl)cyclohexene: b.p. 113-115 °C at 0.1 mm Hg; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.65 (s, 3H), 1.74 (s, 3H), 1.67-1.80 (m, 1H), 1.90-2.27 (m, 9H), 2.76-2.90 (m, 1H), 5.13-5.21 (m, 1H), 5.53 (s, br, 1H), 7.20-7.39 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 17.70, 25.71, 25.83, 26.45, 29.61, 36.81, 37.79, 40.59, 120.47, 124.30, 125.91, 126.86, 128.32, 131.38, 137.45, 147.37 ppm; MS: *m*/*z*: 240 $[M]^+$; elemental analysis (%) calcd for $C_{18}H_{24}$: C 89.94, H 10.06; found: C 89.58, H 10.12.

2-(Butoxymethyl)-1,3-butadiene

A 100 mL round bottomed flask was charged with diethyl ether (30 mL) and lithium diisopropyl amide (1.8 M solution in THF/heptane/ethylbenzene, 33.3 mL, 60 mmol). The mixture was cooled to 0 °C and 2-methyl-2-vinyloxirane [81] (5.75 g, 68 mmol) was added drop wise over 10 min. After one hour, the reaction was concentrated *in vacuo*. To the residue was added DMF (30 mL) followed by *n*-butyl bromide (6.4 mL, 8.2 g, 60 mmol). The reaction was then stirred for 2 days. The mixture was diluted with water (50 mL) and extracted with pentane (2 × 50 mL). The combined pentane layers were washed successively with water (2 × 50 mL), 2 M hydrochloric acid (2 × 25 mL), water (50 mL), saturated sodium bicarbonate (50 mL) and brine (50 mL). The organic layer was dried over anhydrous magnesium sulfate and pentane was removed *in vacuo*. The yellow residual oil consisted of mostly ethyl benzene and the desired product. The oil was purified by flash chromatography (3.5 cm in diameter, 20 cm silica) eluting first with pure pentane (R_f: 0.15) then with 10% diethyl ether in pentane (R_f: 1). This afforded *ca.* 1 g of a yellow oil, which was further purified by distillation (56-59 °C at 12 mm Hg). Yield: 725 mg (7.6%) of a colorless oil. Bp: 56-59 °C at 12 mm Hg. R_f: 0.15 (pentane). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.92 (t, 3H, *J* = 7.3 Hz), 1.30-1.46 (m, 2H), 1.52-1.65 (m, 2H), 3.44 (t, 2H, *J* = 6.6 Hz), 4.14 (s, 2H), 5.07-5.35 (m, 4H), 6.32-6.44 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 13.93, 19.38, 31.82, 70.25, 70.47, 114.23, 116.99, 136.64, 142.74 ppm. MS: 125 1%, 111 1%, 97 3%, 83 17%, 71 15%, 69 15%, 68 100%, 67 79%, 65 17%, 57 54%, 56 30%, 55 40%.

(2*E*,4*E*)-1-Butoxy-2,4-hexadiene

A 100 mL round bottomed flask was charged with DMF (50 mL) and NaH (55% mineral oil suspension, 1.50 g, 34 mmol). Over the course of 10 min, 2,4-hexadien-1-ol (3.42 g, 35 mmol) was added drop wise and the mixture was stirred for an additional 30 min. *n*-Butyl bromide (4.8 g, 35 mmol) was then added drop wise over 5 min followed by stirring for 16 h. The reaction mixture was poured into a 250 mL separatory funnel containing 50 mL of ice-water. The mixture was extracted with pentane (2 × 50 mL) and the combined organic extracts were washed with water (3 × 50 mL). The organic layer was dried with anhydrous magnesium sulfate and pentane was removed *in vacuo*. The slightly yellow residual oil was purified by distillation (88-92 °C at 15 mm Hg) to afford a colorless oil. Yield: 2.56 g (47%). Bp: 88-92 °C at 15 mm Hg. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.91 (t, 3H, *J* = 7.3 Hz), 1.29-1.43 (m, 2H), 1.50-1.61 (m, 2H), 1.74 (d, 3H, *J* = 6.9 Hz), 3.40 (t, 2H, *J* = 6.7 Hz), 3.96 (d, 2H, *J* = 2.9 Hz), 5.56-5.76 (m, 2H), 5.99-6.25 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 13.92, 18.08, 19.34, 31.84, 68.96, 71.16, 127.02, 129.73, 130.83, 132.85 ppm. MS: 154

19%, 139 1%, 125 2%, 111 7%, 98 40%, 97 15%, 83 54%, 81 54%, 80 20%, 79 40%, 70 39%, 69 100%, 67 22%, 57 69%, 56 41%, 55 46%, 53 29%.

(2*E*,4*E*)-2,4-Hexadienyl benzoate

A 100 mL round bottomed flask was charged with pyridine (20 mL) and cooled to 0 °C. Benzoyl chloride (3.23 g, 23 mmol) was added slowly followed by drop wise addition of 2,4-hexadien-1-ol (1.5 g, 15.3 mmol) over 5 min. The ice bath was removed and the reaction was stirred for 16 h. The solution was slowly poured into a beaker containing 250 mL of ice cold 2 M hydrochloric acid. The resulting mixture was extracted with dichloromethane (4 × 60 mL) and the combined organic extracts were washed successively with 4 M hydrochloric acid (2 × 60 mL) and saturated sodium bicarbonate (3 × 60 mL). The organic phase was dried over anhydrous magnesium sulfate and dichloromethane was removed *in vacuo*. The residue was purified by flash chromatography (EtOAc 1, heptane 4) to afford a colorless oil. Yield: 2.83 g (91%). Bp: 133-134 °C at 3 mm Hg (lit. [82] bp: 130 °C at 1 mm Hg). R_f: 0.47 (EtOAc 1, heptane 4). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.77 (d, 3H, *J* = 3.4 Hz), 4.83 (d, 2H, *J* = 3.3 Hz), 5.69-5.86 (m, 2H), 6.03-6.15 (m, 1H), 6.29-6.40 (m, 1H), 7.40-7.47 (m, 2H), 7.52-7.60 (m, 1H), 8.03-8.09 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 18.13, 65.39, 123.70, 128.28, 129.57, 130.24, 130.40, 131.30, 132.85, 134.91, 166.34 ppm. MS: 202 5%, 173 2%, 122 8%, 106 8%, 105 100%, 80 24%, 79 62%, 77 61%, 51 25%. NMR data are in accordance with literature values [82].

***tert*-Butyl((2*E*,4*E*)-2,4-hexadienyloxy)diphenylsilane**

A 250 mL round bottomed flask was charged with CH_2Cl_2 (100 mL), 2,4-hexadien-1-ol (3.0 g, 30.6 mmol) and imidazole (4.2 g, 61.3 mmol). The mixture was stirred followed by addition of *tert*-butylchlorodiphenylsilane (12.6 g, 45.9 mmol) and stirring for an additional 16 h.The reaction was diluted with diethyl ether (100 mL) and washed with 1 M hydrochloric acid (100 mL) and brine (100 mL). Removal of the solvents *in vacuo* afforded 14.38 g of a crude product which was purified by flash chromatography (EtOAc 1, heptane 4) to give a colorless oil. Yield: 9.48 g (92%). R_f: 0.51 (EtOAc 1, heptane 4). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.11 (s, 9H), 1.79 (d, 3H, *J* = 3.4 Hz), 4.27 (d, 2H, *J* = 2.6 Hz), 5.63-5.78 (m, 2H), 6.05-6.17 (m, 1H), 6.22-6.34 (m, 1H), 7.38-7.50 (m, 6H), 7.70-7.77 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 18.11, 19.22, 26.80, 64.22, 127.61, 128.95, 129.40, 129.57, 130.10, 131.02, 133.69, 135.52 ppm. MS: 280 7%, 279 27%, 200 19%, 199 100%, 181 9%, 77 26%, 57 14%.

3,4-Dimethyl-3-cyclohexene-1-carbaldehyde (prepared in diglyme)

A 50 mL round bottomed flask was charged with diglyme (30 mL), 2,3-dimethyl-1,3-butadiene (2.54 g, 30.0 mmol) and acrolein (3.0 mL, 45 mmol) followed by addition of $BF_3{\cdot}OEt_2$ (0.19 mL, 1.5 mmol, 5%) under stirring. The reaction was stirred at room temperature (water bath) for 10 min. The reaction mixture was transferred to a 250 mL separatory funnel containing saturated sodium bicarbonate (50 mL) and pentane (50 mL). The phases were separated and the organic phase was washed with saturated sodium bicarbonate (50 mL) and water (3 × 50 mL) and then dried over anhydrous sodium sulfate. Pentane was removed *in vacuo* and the residual, slightly cloudy oil purified by distillation (85-87 °C at 15 mm Hg). Yield: 3.70 g (89%). Bp: 85-87 °C at 15 mm Hg (lit. [77] bp: 92-94 °C at 25 mm Hg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.54-1.68 (m, 7H), 1.86-2.24 (m, 5H), 2.40-2.52 (m, 1H), 9.67 (d, 1H, *J* = 0.7 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 18.92, 19.05, 22.82, 30.13, 30.50, 46.95, 123.42, 125.84, 204.81 ppm. MS: 138 53%, 123 25%, 109 55%, 107 41%, 105 31%, 95 39%, 93 31%, 91 43%, 81 34%, 79 46%, 77 28%, 67 100%, 55 39%. NMR data are in accordance with literature data [77].

3,4-Dimethyl-3-cyclohexene-1-carbaldehyde (prepared in diethyl ether)

A 100 mL round bottomed flask was charged with diethyl ether (50 mL), 2,3-dimethyl-1,3-butadiene (4.23 g, 50 mmol) and acrolein (5.0 mL, 75 mmol) followed by addition of $BF_3{\cdot}OEt_2$ (0.32 mL, 2.5 mmol, 5%) under stirring. The reaction was stirred at room temperature (water bath) for 10 min. The reaction mixture was transferred to a 250 mL separatory funnel containing saturated sodium bicarbonate (50 mL). The phases were separated and the organic phase was washed with saturated sodium bicarbonate (50 mL) and water (50 mL) and then dried over anhydrous sodium sulfate. Diethyl ether was removed *in vacuo* and the residual, slightly cloudy oil purified by distillation (85-87 °C at 15 mm Hg). Yield: 6.02 g (87%).

1,3,4-Trimethyl-3-cyclohexene-1-carbaldehyde

A 50 mL round bottomed flask was charged with diglyme (20 mL), 2,3-dimethyl-1,3-butadiene (1.64 g, 19.4 mmol) and methacrolein (2.5 mL, 30 mmol) followed by addition of $BF_3{\cdot}OEt_2$ (0.25 mL, 2.0 mmol, 10%) under stirring. The reaction was stirred at room temperature (water bath) for 1 h.The reaction mixture was transferred to a 250 mL separatory funnel containing saturated sodium bicarbonate (50 mL) and pentane (50 mL). The phases were separated and the organic phase was washed with saturated sodium bicarbonate (50 mL) and water (3 × 50 mL) and then dried over anhydrous sodium sulfate. Pentane was removed *in vacuo* and the residual, slightly cloudy oil purified by distillation (89-81 °C at 18 mm Hg). Yield: 2.80 g (95%). Bp: 89-91 °C at 18 mm Hg. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.02 (s, 3H), 1.39-1.52 (m, 1H), 1.58 (s, 3H), 1.63 (s, 3H), 1.69-1.83 (m, 2H), 1.91-2.01 (m, 2H), 2.19-2.29 (m, 1H), 9.45 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 18.77, 19.18, 20.70, 28.40, 29.20, 37.81, 45.24, 122.98, 125.07, 206.22 ppm. MS: 152 22%, 137 18%, 123 54%, 109 78%, 91 32%, 82 37%, 81 75%, 67 100%, 55 46%. NMR data are in accordance with literature values [83].

3,4,6-Trimethyl-3-cyclohexene-1-carbaldehyde

A 50 mL round bottomed flask was charged with diglyme (20 mL), 2,3-dimethyl-1,3-butadiene (1.68 g, 19.8 mmol) and crotonaldehyde (2.5 mL, 30 mmol) followed by addition of $BF_3 \cdot OEt_2$ (0.25 mL, 2.0 mmol, 10%) under stirring. The reaction was stirred at room temperature for 6 h. The reaction mixture was transferred to a 250 mL separatory funnel containing saturated sodium bicarbonate (50 mL) and pentane (50 mL). The phases were separated and the organic phase was washed with saturated sodium bicarbonate (50 mL) and water (3 × 50 mL) and then dried over anhydrous sodium sulfate. Pentane was removed *in vacuo* and the residual, slightly cloudy oil was purified by distillation (91-92 °C at 14 mm Hg). Yield: 2.68 g (89%). Bp: 91-92 °C at 14 mm Hg (lit. [84] bp: 89 °C at 12 mm Hg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.99 (d, 3H, *J* = 3.2 Hz), 1.59 (s, 3H), 1.63 (s, 3H), 1.64-1.77 (m, 1H), 1.90-2.25 (m, 5H), 9.60 (d, 1H, *J* = 1.5 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 18.64, 18.85, 19.55, 28.75, 30.30, 38.88, 53.49, 122.55, 125.07, 205.34 ppm. MS: 152 44%, 137 12%, 123 30%, 121 100%, 119 29%, 110 27%, 109 28%, 107 55%, 105 37%, 95 39%, 91 44%, 81 69%, 79 41%, 67 92%, 55 58%.

3,4-Dimethyl-6-phenyl-3-cyclohexene-1-carbaldehyde

A 50 mL round bottomed flask was charged with diglyme (20 mL), 2,3-dimethyl-1,3-butadiene (1.65 g, 19.5 mmol) and cinnamaldehyde (3.8 mL, 30 mmol) followed by addition of $BF_3 \cdot OEt_2$ (0.38 mL, 3.0 mmol, 15%) under stirring. The reaction was stirred at room temperature for 24 h. The reaction mixture was transferred to a 250 mL separatory funnel containing saturated sodium bicarbonate (50 mL) and pentane (50 mL). The phases were separated and the organic phase was washed with saturated sodium bicarbonate (50 mL) and water (3 × 50 mL) and then dried over anhydrous sodium sulfate. Pentane was removed *in vacuo* and the residual oil purified by flash chromatography (EtOAc 1, heptane 19). Yield: 3.19 g (74%). Bp: 110-113 °C at 0.1 mm Hg (lit. [85] bp: 171-173 °C at 3.5 mm Hg). R_f: 0.25 (EtOAc 1, heptane 19). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.66 (s, 3H), 1.70 (s, 3H), 1.99-2.37 (m, 4H), 2.74-2.87 (m, 1H), 3.02-3.15 (m, 1H), 7.17-7.36 (m, 5H), 9.47 (d, 1H, *J* = 1.5 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 18.73, 18.75, 30.98, 39.42, 41.37, 52.00, 123.33, 125.56, 126.66, 127.37, 128.69, 143.42, 204.48 ppm. MS: 214 40%, 199 3%, 183 55%, 172 33%, 131 32%, 115 29%, 95 40%, 94 61%, 91 100%, 82 50%, 77 37%, 67 97%.

Pd/HT

To a 100 mL aqueous solution containing 0.10 mmol of $Na_2[PdCl_4]$ is added 1.000 g of hydrotalcite in one portion under vigorous stirring. After 15 minutes of stirring, it appears that most of the $PdCl_4^{2-}$ has been immobilized (the solution has become colorless). The suspension is stirred for 12 hours at room temperature. The mixture was then filtrated and washed with 500 mL of water in small portions. It is then dried for 8 hours in the desiccator and crushed in a mortar to afford 959 mg of Pd(II)/HT. Reduction is done directly in the reaction flask by first dehydrating the catalyst (150 °C, vacuum, 30 minutes) and then reducing using H_2 (150 °C, 1 atm H_2, 30 minutes). This affords a grey powder which is the palladium nanoparticle catalyst.

Pd/HAP and Pd/TiO_2

33.2 mg $Pd(CF_3CO_2)_2$ (0.10 mmol) is dissolved in 100 ml water in a 100 ml roundbottomed flask with the aid of ultrasonication. Under vigorous stirring, 1.000 g of hydroxyapatite (HAP) or TiO_2 is added. The mixture is stirred for 12 hours at room temperature. Then filtrated and washed with 500 ml of water in small portions. It is then dried for 8 hours in the desiccator and crushed in a mortar to afford the Pd(II)/HAP and Pd(II)/TiO_2. Reduction is done directly in the reaction flask by first dehydrating the catalyst (150 °C, vacuum, 30 minutes) and then reducing using H_2 (150 °C, 1 atm H_2, 30 minutes). This affords a grey powder which is the palladium nanoparticle catalyst. Pd/HAP and Pd/TiO_2 were also obtained by KBH_4 reduction. Thus, 200 mg Pd/HAP or Pd/TiO_2 were added to a vigorously stirred solution of 10.8 mg KBH_4 in 100 ml water. Immediate reduction occurs, and the mixture is stirred for one hour. Filtration, wash with water and drying in the desiccator affords a grey powder which is the Pd/HAP and Pd/TiO_2.

Decarbonylating procedure using palladium nanoparticle catalysts

A 30 mL Schlenk flask containing 100 mg catalyst is charged with 156.2 mg 2-naphthaldehyde (1.00 mmol, recryst from ethanol) and biphenyl (ca. 1.0 mmol, internal standard). The flask is then evacuated and filled with argon and finally 5.0 mL solvent is added (xylene or mesitylene, dried over Na). The flask is then placed in a 150 °C (xylene) or 185 °C (mesitylene) hot oil bath and stirred vigorously. GC-samples are acquired frequently. The catalyst recycle study is done by centrifugation of the reaction mixture and washing of the catalyst with acetone. The catalyst is then dried in vacuum and used as above.

4. Aerobic Oxidations using Gold Nanoparticles

Gold has been known since the ancient times and has been desired and awed due to its metallic lustre and inertness towards corrosion. This inertness has also led chemists to believe that gold is a catalytically dead metal. However in recent years gold has been found to display a high catalytic activity for the aerobic oxidation of various substrates when dispersed in the form of nanoparticles.

Oxidation reactions in general are highly important in many areas of chemistry. In many cases heavy metal oxidants are still in use due to their long record of reliance. However, from the viewpoint of green chemistry, oxygen is a much more attractive oxidant since water is the only by-product formed. Gold nanoparticle catalysts are interesting because they can facilitate the use of oxygen as an oxidant in many basic oxidation reactions.

4.1 Background on gold catalysis

The modern gold-rush was sparked by two discoveries that changed the picture of gold as being catalytically dead. The first discovery was made by Graham Hutchings who was able to predict and show that gold is the most active metal catalyst for the hydrochlorination of acetylene to form vinyl chloride [86]. Two years later, in 1987 Masatake Haruta discovered that gold nanoparticles supported on metal oxides such as α-Fe_2O_3 are highly active catalysts for the oxidation of CO to form CO_2 at very low temperatures (-70 ºC) [87-88]. Since then, gold has been applied as catalyst for a large number of reactions and several thorough reviews have been made on this topic [89-92].

By definition, gold nanoparticles are particles smaller than 200 nm in size. However only gold nanoparticles smaller than 10 nm are highly active as oxidation catalysts. Supported gold nanoparticles are typically used rather than the "naked" gold colloids themselves, although gold colloids are known to be catalytically active [93]. The support stabilizes the gold nanoparticles and prevents sintering to form large and inactive gold particles. Supported gold nanoparticle catalysts can be prepared using different methods. One method is based on the immobilization of preformed gold colloids on a support (deposition method). Another procedure involves neutralization of $HAuCl_4$ with small amounts of base to precipitate Au_2O_3 directly onto a support followed by reduction or calcination to form gold nanoparticles (impregnation method). The size distribution is typically determined by TEM measurement (transmission electron microscopy), wherein individual gold nanoparticles can be observed and measured (figure 4.1).

The active nature of nano gold has been studied *in silico* by Nørskov *et al.* [94]. Here, low-coordinated Au-corners on small gold clusters are identified as possible active sites (figure 4.1). These low-coordinated sites have the capability of binding oxygen more strongly than gold on extended surfaces and are thereby able to activate oxygen in oxidation reactions.

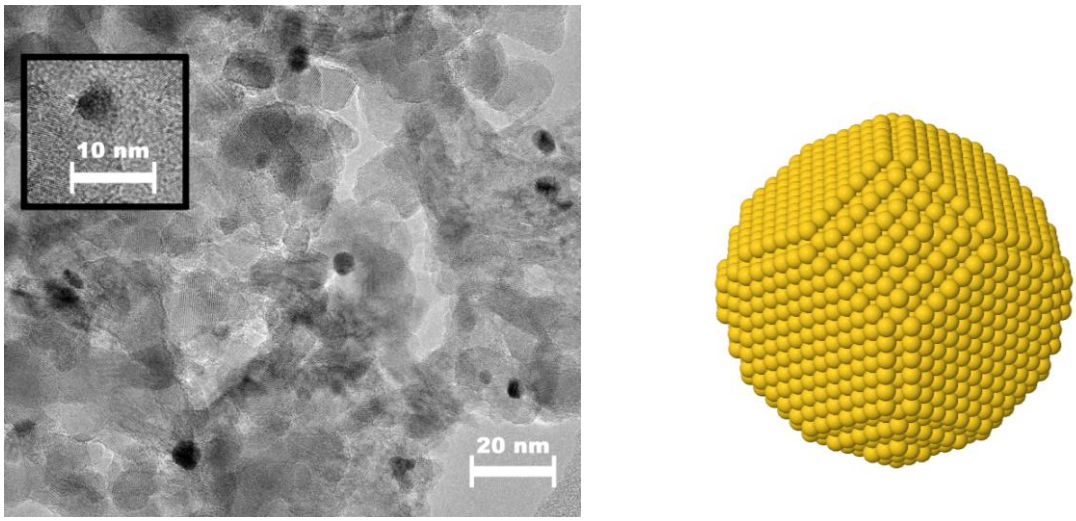


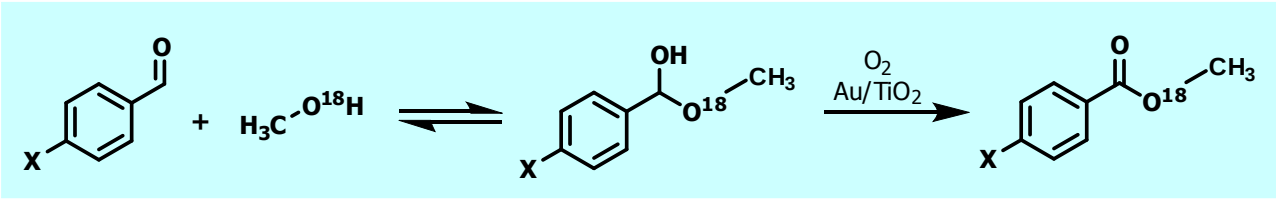
Figure 4.1 Left: TEM image of Au/spinel [34]. The black dots are the solid gold nanoparticles. In this case they are about 5 nm in diameter. Right: illustration of a gold nanoparticle and its corners which are capable of binding oxygen.

4.1.1 Gold nanoparticles and alcohol oxidation

In 1998 Prati and Rossi reported that carbon supported gold nanoparticles are capable of catalyzing the oxidation of diols in aqueous phase using oxygen as the stoichiometric oxidant [95]. This is the first report of gold catalyzing alcohol oxidation, and in this report gold is superior to conventional palladium and platinum catalysts. Later work by Hutchings demonstrated that Au/C is also capable of oxidizing a basic aqueous glycerol solution to form sodium glycerate with 100% selectivity at 56% conversion [96-97]. Corma and co-workers have successfully used nanocrystalline ceria as support for the gold nanoparticles to facilitate the oxidation of primary alcohols to carboxylic acids, without the addition of base [98].

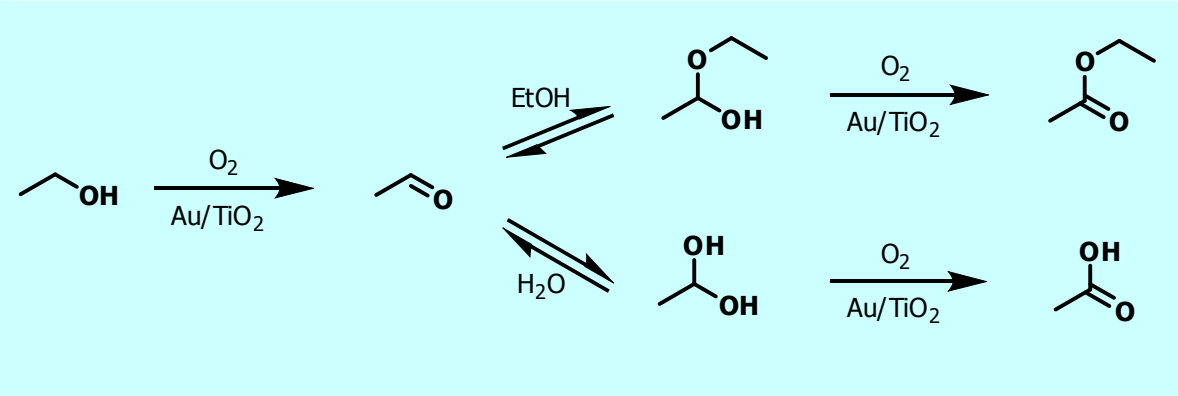
The reaction mechanism for the oxidation of alcohols to form aldehydes has been studied recently by our group using a Hammett approach [99]. Here a negative slope of the Hammett plots reveals that a partial positive charge is being built up in the rate determining step. This suggests that the oxidation proceeds via hydride abstraction. Likewise the mechanism for the oxidation of aldehydes to form methyl esters have been studied recently [100]. Here a positive slope was found in the Hammett plot, suggesting that a partial negative charge is being built up in the rate determining step.

Isotopic labelling by using O^{18}-labelled oxygen and O^{18}-labelled methanol as solvent revealed that the oxygen incorporated into the product methyl ester originates from methanol and not from O_2. This evidently points towards the formation of a hemiacetal of the aldehyde and methanol, which then subsequently is oxidized to the methyl ester (scheme 4.1). The negative charge being built up in the rate determining step when oxidizing aldehydes could thus result from the hemiacetal formation being the rate limiting step.



Scheme 4.1

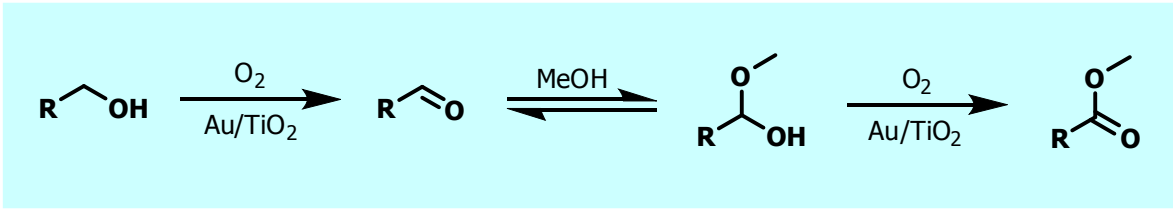
However, before these studies were undertaken we first had to pioneer a procedure for oxidizing alcohols and aldehydes to methyl esters. We became interested in such a procedure, since it was discovered in our group that by the use of a Au/spinel catalyst it is possible to oxidize ethanol to acetic acid at temperatures of 180 ºC with a 35 bar air pressure [34]. An interesting observation in this procedure was that small amounts of acetaldehyde and ethyl acetate are formed as by-products. This indicates that the reaction pathway involves oxidation of ethanol to acetaldehyde followed by hydration with water or hemiacetalization with ethanol and subsequent oxidation to form either acetic acid or ethyl acetate (Scheme 4.2).



Scheme 4.2

Based on this reaction pathway we speculated that if methanol is used as reaction media rather than water, the dominant reaction route would be hemiacetalization of the aldehyde with methanol

followed by oxidation to directly form a methyl ester (Scheme 4.3). This procedure will only be possible if a primary alcohol such as ethanol is oxidized much faster than methanol, since otherwise extensive methanol loss would occur from oxidation. However, based on the fact that methanol has a higher oxidation potential than other alcohols [101], it seemed plausible that only a limited methanol loss would occur.



Scheme 4.3

The remaining part of this chapter describes the development of a gold catalyzed oxidative esterification procedure and its application on several substrates.

4.2 Results and discussion[†]

A reference 1 wt% Au/TiO_2 catalyst acquired from the World Gold Council was used for these oxidative esterification studies. The size of the gold nanoparticles is determined by TEM and 95% of the particles are in range of 2-5 nm in size. The oxidation experiments take place at 130 ºC in an autoclave pressurized with an O_2 partial pressure of 9.2 bar, corresponding to an O_2-substrate ratio of 7:1 (7x excess). Several parameters were studied in order to find a useful procedure to convert primary alcohols to methyl esters in one reaction. Base is well known to act as a promoter for gold in oxidation reactions [102], and therefore the effect of adding sodium methoxide to the reaction mixture was studied. The methanol to substrate molar ratio was also studied as well as the time needed to achieve full conversion was determined.

4.2.1 The promoting effect of base

Initially 1-hexanol was oxidized in an excess of methanol (1:19 ratio) for 24 hours. Using this procedure, an 89% GC-yield of methyl hexanoate was achieved. The addition of base was soon discovered to have a beneficial role by increasing the rate of the reaction. Shorter time-frames of 1 hour were therefore used instead to evaluate the effect of base-addition of the reaction rate (table 4.1).

Evidently, the addition of base increases the rate of reaction significantly. We therefore decided to use 2 mol% of sodium methoxide as additive, since this value seems to give a good compromise

Substrate	Reaction time (h)	$NaOCH_3$ additive (mol%)	Product	Conv. (%)	Yield (%)
1-hexanol	1	0.2	Methyl hexanoate	56	52
1-hexanol	1	2	Methyl hexanoate	60	52
1-hexanol	1	10	Methyl hexanoate	85	81

Table 4.1. Effect of the addition of base on the rate of 1-hexanol oxidation. Au/substrate ratio is 1:625, substrate/MeOH ratio is 1:19, reaction performed at 130 ºC using a 9.2 bar of O_2 partial pressure. Yield and conversion determined by GC.

between rate acceleration and at the same time minimizing the base amount. Side reactions stemming from Claisen condensation of the ester product was not observed. The exact role of the base is unknown, but possible explanations could be that the base assists in the formation of an alcoxide ion which binds more strongly to the gold surface that the neutral alcohol [97]. Another explanation is that base increases the rate of hemiacetal formation which is needed prior to the final oxidation step leading to the methyl ester.

4.2.2 Methanol to substrate ratio

Different methanol-to-substrate molar ratios were examined when using 2 mol% sodium methoxide as additive (figure 4.2).

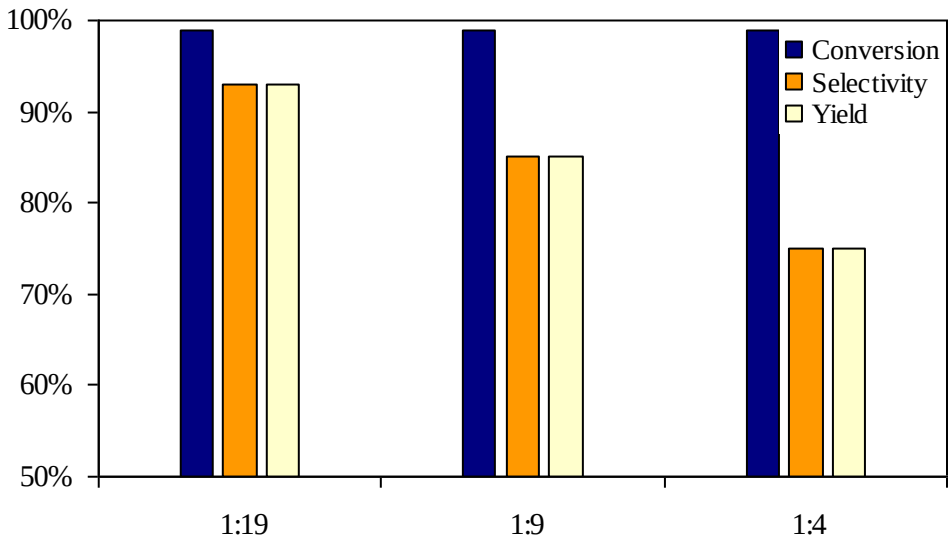
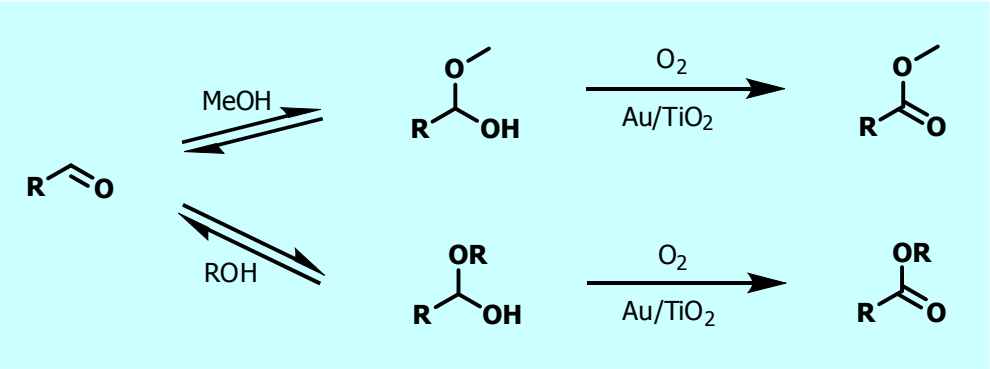


Figure 4.2. Effect of the hexanol to methanol molar ratio on the selectivity towards methyl hexanoate. Au/substrate ratio is 1:625, substrate/MeOH ratio is 1:19, 1:9 and 1:4, reaction performed at 130 ºC using a 9.2 bar of O_2 partial pressure. The reaction time is 24 hours. Yield and conversion determined by GC.

This examination showed that the alcohol ratio has a large influence on the product selectivity, since a small excess of methanol will only lead to low selectivity of the desired methyl ester. When a small excess of methanol is used, hexyl hexanoate is formed in large amounts, suggesting that a competition between methanol and 1-hexanol is in effect in the hemicacetal formation step leading to either product (Scheme 4.4).



Scheme 4.4

4.2.3 Final fine-tuning of the reaction conditions

With the amount of base additive set to 2 mol% and the methanol-to-substrate ratio set to 19:1, a final fine-tuning of the reaction was done in order to find a suitable reaction time (table 4.2). Indeed it is possible to lower the reaction time from 24 hours to 10 hours without a loss in methyl ester yield.

Substrate	Reaction time (h)	$NaOCH_3$ additive (mol%)	Product	Conv. (%)	Yield (%)
1-hexanol	24	2	Methyl hexanoate	>99	93
1-hexanol	10	2	Methyl hexanoate	97	93 (79)
1-hexanol	6	2	Methyl hexanoate	96	91

Table 4.2. Effect of the reaction time on the yield of methyl hexanoate. Au/1-hexanol ratio is 1:625, 1-hexanol/MeOH ratio is 1:19, reaction performed at 130 ºC using a 9.2 bar of O_2 partial pressure and 2 mol% sodium methoxide relative to 1-hexanol. Yield and conversion determined by GC, yield in parenthesis is isolated yield.

4.2.4 Use of other alcohols

The procedure was applied to a few different primary alcohols (table 4.3). In all cases good to excellent GC-yield is obtained and the methyl esters were all isolated in good yields.

This procedure thus seems to be a useful tool for the direct conversion of primary alcohols to methyl esters [103], and it is a green alternative to reagents such as iodine, trichloroisocyanuric acid and (diacetoxy)iodobenzene which have been used for this type of transformation [104-106].

Substrate	Reaction time (h)	$NaOCH_3$ additive (mol%)	Product	Conv. (%)	Yield (%)
Benzyl alcohol	10	2	methyl benzoate	>99	>99 (79)
Cinnamyl alcohol	10	2	methyl cinnamate	>99	88 (76)
2-(hydroxymethyl) pyridine	10	2	methyl pyridine-2-carboxylate	95	95 (85)

Table 4.3. Application of the procedure to other alcohols. Au/substrate ratio is 1:625, substrate/MeOH ratio is 1:19, reaction performed at 130 ºC using a 9.2 bar of O_2 partial pressure and 2 mol% sodium methoxide relative to 1-hexanol. Yield and conversion determined by GC, yields in parenthesis are isolated yields.

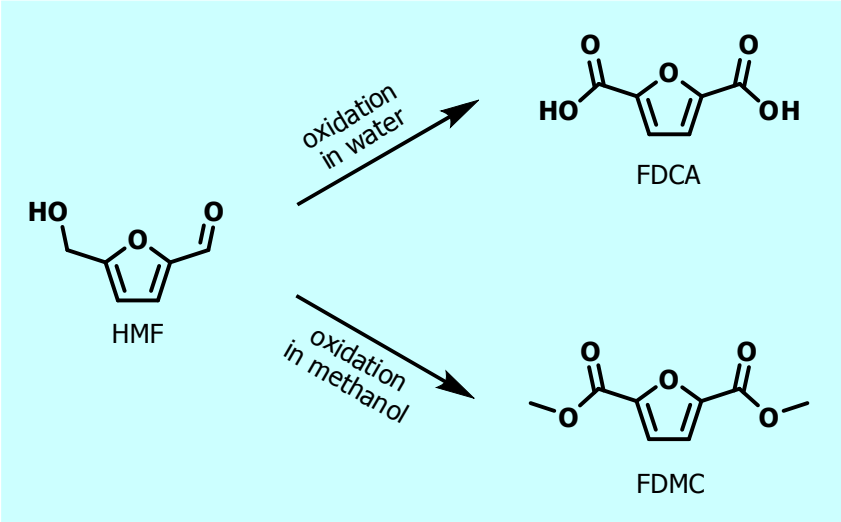
Furthermore, only a small amount of base additive is needed, whereas when alcohols are oxidized in water using gold catalysts, typically super-stoichiometric amounts of base are needed since the formed carboxylic acid will neutralize one equivalent of the base [96-97, 107]. In addition, methyl esters are easy to purify compared with many carboxylic acids, since a simple distillation will often suffice.

However, a loss of methanol does occur from over-oxidation during the reaction and this is the drawback of this methodology. This is evident from GC-analysis of the gas-phase after an oxidation experiment in which 1-hexanol is oxidized for 24 hours using 2 mol% sodium methoxide as promoter. Here, the gas-phase was found to contain 78% CO_2. The methanol loss in this reaction corresponds to 1-3 moles of methanol per mole of methyl ester formed.

4.3 Oxidation of renewable building blocks

With a useful procedure for oxidizing primary alcohols to methyl esters in hand, we decided to initiate a more broad application of the method. We chose to look into converting 2-hydromethyl fufural (HMF) and furfural into useful chemicals.

HMF, as mentioned in chapter 2, can be made from fructose by acid catalyzed dehydration. HMF itself has little or no use, but through oxidation or hydrogenation it can be converted into furan 2,5-dicarboxylic acid (FDCA) and 2,5-dihydroxymethyl furan, respectively. Naturally we were interested in oxidizing HMF directly to form the di-ester furan 2,5-dimethylcarboxylate (FDMC) (scheme 4.5).



Scheme 4.5

This ester is equally interesting as the acid for its potential use as a polymer building block. In fact the ester is probably more interesting in some aspects, since it is much easier to purify the ester than the carboxylic acid.

4.3.1 HMF and furfural

A procedure specific for HMF, based on the previous described oxidative esterification procedure was developed. Using a methanol/HMF ratio of 79:1 and a O_2-partial pressure of 4 bar and 8 mol% sodium methoxide as additive, it was possible to convert HMF to FDMC within a time-frame of 3 hours at 130 ºC. By performing independent oxidation experiments, a time-profile of the reaction was made (figure 4.3).

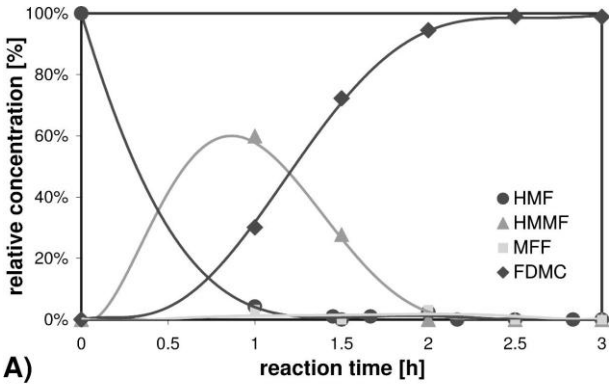
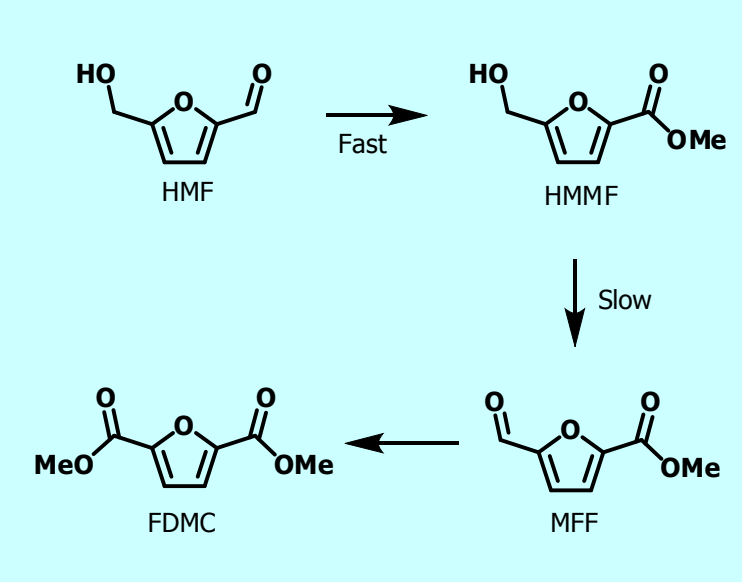


Figure 4.3. Time profile of the gold catalyzed oxidation of HMF using Au/TiO_2. Au/HMF ratio is 1:313, HMF/MeOH ratio is 1:79 and 8 mol% of sodium methoxide is used. The reaction is carried out in an autoclave at 130 ºC with an oxygen pressure of 4 bar.

This profile shows that HMF is almost completely converted within just one hour and that a build-up of 5-hydroxymethyl methylfuroate (HMMF) is taking place, indicating that the aldehyde moiety is oxidized faster than the primary alcohol group (scheme 4.6). In fact, if the oxidation reaction is performed at room temperature with just 1 bar of O_2, HMMF is formed in more than 90% yield after just 3 hours, illustrating that alcohol oxidation only takes place at elevated temperatures. Similarly, furfural was oxidized at room temperature to give an 85% yield of methyl furoate after 5 hours.



Scheme 4.6

In summary, using gold-catalyzed oxidative esterification HMF can be converted into the dimethyl ester FDMC in good yields and this is therefore an interesting alternative to oxidizing HMF in water to form furan 2,5-dicarboxylic acid [108]. FDMC was purified by sublimation to afford colourless crystals. The sublimation takes place even at moderate conditions (160 ºC, 1 atm), thereby illustrating the benefit of producing the volatile esters instead of acids.

4.4 Oxidation of aldehydes under mild conditions

Fascinated by the ability of gold to oxidize aldehydes at room temperature to form high yields of *e.g.* methyl furoate, we decided to look further into oxidizing aldehydes. We were particularly interested in examining the activity of the gold catalyst at low temperatures.

The low-temperature oxidation of benzaldehyde was examined using a benzaldehyde to methanol ratio of 1:30 together with 10 mol% sodium methoxide. Oxidation reactions were performed in an open system, *i.e.* the O_2-partial pressure is 0.2 bar. The gold-catalyst used for this study was a 1 wt% Au/TiO_2 supplied by Mintek. Full conversion of benzaldehyde to form methyl benzoate is achieved at room temperature and at 40 ºC in less than one hour using a Au:substrate ratio of 1:500. Interestingly, at temperatures as low as -20 ºC and -78 ºC, oxidation of benzaldehyde still takes place, illustrating the high activity of gold nanoparticles for this type of oxidation reaction (figure 4.4).

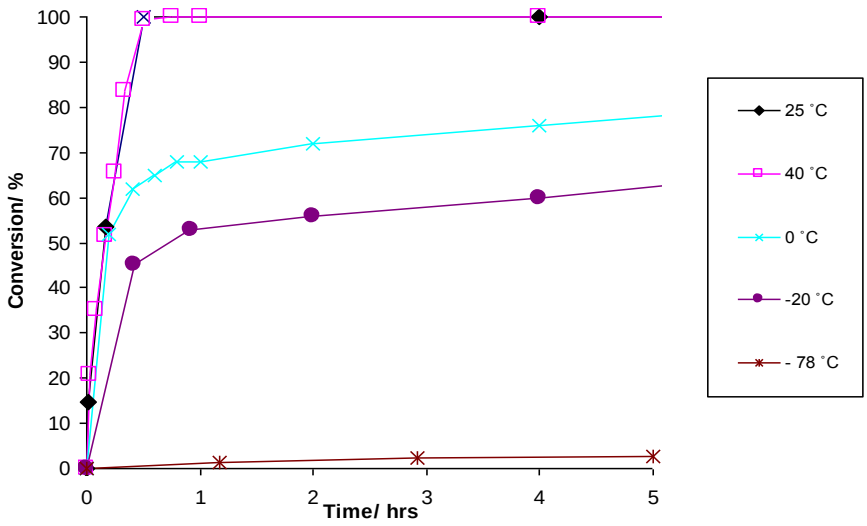


Figure 4.4. Oxidative esterification of benzaldehyde to form methyl benzoate at different temperatures. Benzaldehyde:Methanol 1:30, Au/benzaldehyde is 1:500 and 10 mol% sodium methoxide is used. The catalyst is a 1 wt % Au/TiO_2 from Mintek, and normal air atmosphere is used.

Again, the role of sodium methoxide is to increase the rate of the reaction as illustrated in figure 4.5. In the absence of sodium methoxide full conversion takes about 30 hours to reach as compared to less than one hour when using 10 mol%.

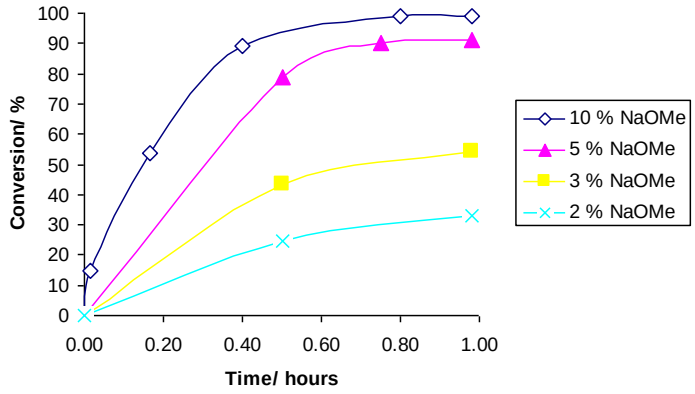
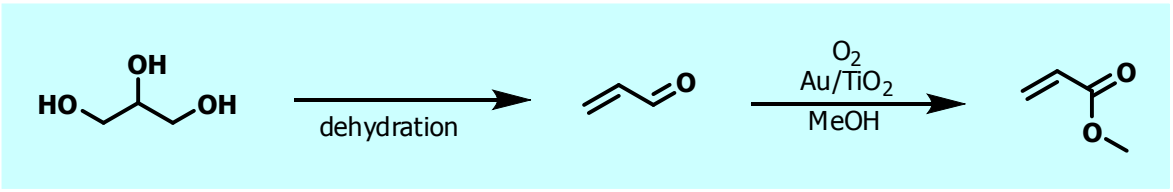


Figure 4.5. Oxidative esterification of benzaldehyde to form methyl benzoate at room temperature using different base additive amounts. Benzaldehyde:Methanol 1:30, Au/benzaldehyde is 1:500. The catalyst is a 1 wt % Au/TiO_2 from Mintek, and normal air atmosphere is used.

4.4.1 Acrolein to methyl acrylate

Methyl acrylate is a highly important commodity chemical that is currently produced from the oxidation of propylene. We therefore wanted to investigate the oxidation of acrolein, using this methodology, to form methyl acrylate.

Due to the incompatibility of acrolein with strong bases, the oxidation reaction was performed in the absence of any additives. This demanded a much longer reaction time, but by increasing the reaction time to 40 hours, it was possible to convert acrolein directly into methyl acrylate by oxidizing it in methanol (1:80 molar ratio) at 25 ºC with an air atmosphere (scheme 4.7). A 87% yield of methyl acrylate was achieved in this way, thereby illustrating the possibility of making valued added chemicals from glycerol, by first dehydrating it to acrolein followed by an oxidative esterification reaction.



scheme 4.7

4.5 Oxidation of glycerol

A final example of how gold nanoparticles can be used for the conversion of biomass into value added chemicals is the direct oxidation of glycerol and diols. As mentioned previously, Hutchings

have studied the aqueous phase oxidation of glycerol to form sodium glycerate [96-97] and Prati and Rossi studied the oxidation of 1,2-propanediol to form sodium lactate in up to 78% yield [95]. We were particularly interested in oxidizing glycerol in methanol to form methyl esters. Interestingly, glycerol produced from transesterification of triglycerices in the production of biodiesel contains both methanol and sodium methoxide. Therefore this by-product stream can easily be envisioned as a valuable resource if useful chemicals can be made from it.

4.5.1 Oxidation procedure

Oxidation at the same temperature used previously (130 ºC) was found to cause C-C bond breakage of the glycerol substrate. Therefore lower temperatures had to be used in this case. A 1:59 glycerol-to-methanol ratio was used together with a 10 mol% sodium methoxide relative to glycerol. Two different World Gold Council reference catalysts were examined, 1 wt% Au/TiO_2 and 1 wt% Au/Fe_2O_3, the Au:glycerol ratio is in both cases 1:112. The oxidation experiments were performed in an autoclave at 100 ºC using an O_2-partial pressure of 4.4 bar.

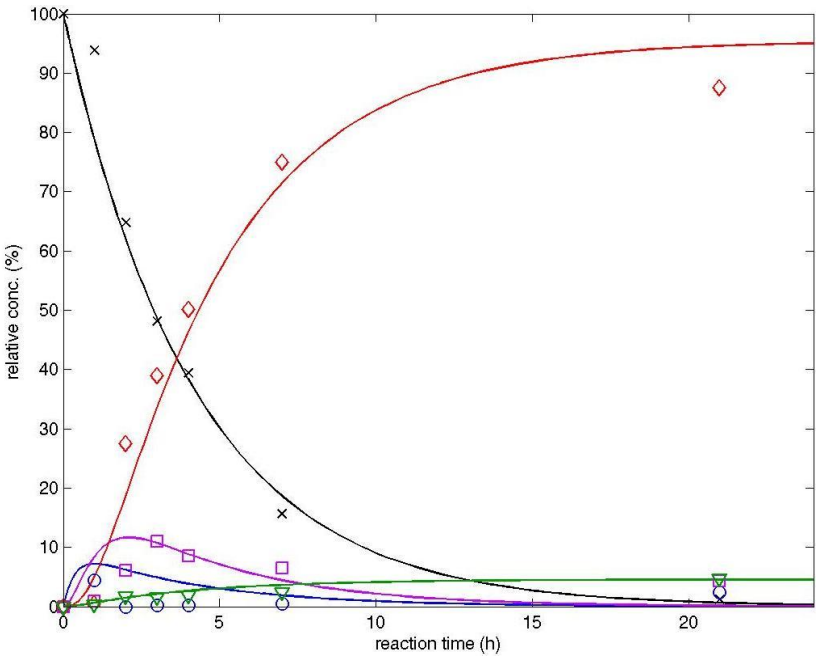
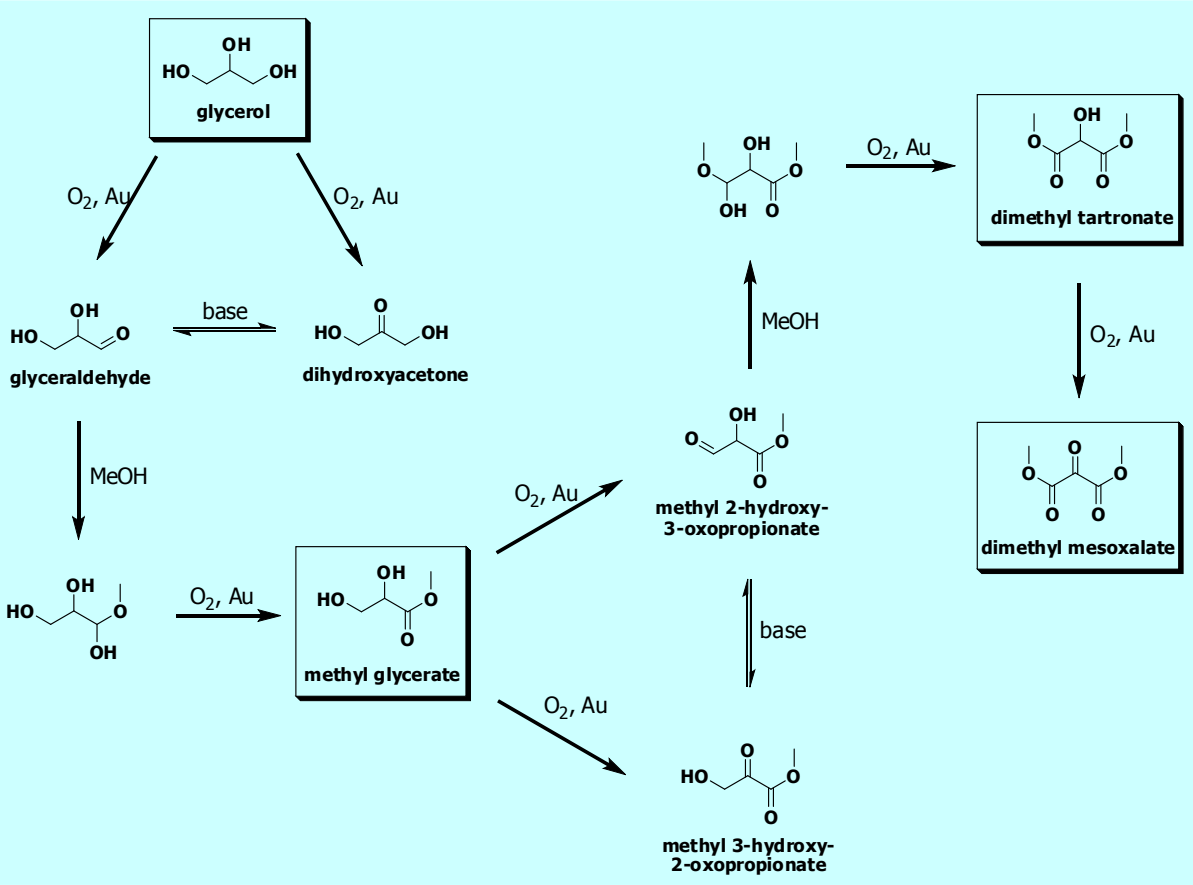


Figure 4.6. Oxidative esterification of glycerol with the use of 1% Au/Fe_2O_3 at 100ºC. Methanol:glycerol was 59:1, Au:glycerol was 1:112. A O_2-partial pressure of 4.4 bar was used. 10% $NaOCH_3$ relative to glycerol was used. Legend: glycerol: –×– , methyl glycerate: –o– , dimethyl tartronate: –□– dimethyl mesoxalate: –◊– , methyl glycolate: –▽–

Using these conditions, glycerol was oxidized to give dimethyl mesoxalate in up to 89% GC-yield at full conversion for the Au/Fe_2O_3 catalyst (scheme 4.8). The Au/TiO_2 catalyst was slightly less selective and gave 79% of dimethyl mesoxalate. A time profile of the reaction showed that several intermediate products are formed and disappear during the reaction (figure 4.6). Methyl glycerate is observed as an initial product, corresponding to partial oxidation of glycerol. Dimethyl tartronate is also observed, which is formed by further oxidation of methyl glycerate as well as final oxidation to furnish dimethyl mesoxalate. Some products are not observed, such as glyceraldehyde and dihydroxyacetone. These products are most likely formed, but are probably converted very fast and are thus not observable. Some C-C scission does take place during the reaction as methyl glycolate is formed in about 5% yield. A possible reaction pathway is shown in scheme 4.8.

4.5.2 Oxidation of 1,2- and 1,3-propanediol

By employing the same approach, 1,2-propanediol was oxidized using Au/TiO_2 in methanol to form methyl lactate in a 72% yield at full conversion. Here 1-hydroxyacetone was observed by GC as the



Scheme 4.8

initial product, and further conversion to methyl lactate must involve tautomerisation to lactaldehyde followed by oxidative esterification. C-C scission also takes place in this case, as methyl acetate is formed in a 21% yield after 21 hours.

Likewise 1,3-propanediol was oxidized to form methyl 3-hydroxypropionate in 85% yield together with small amounts (5%) of methyl acrylate stemming from dehydration. Here, no products formed by C-C bond breakage were observed, suggesting that this side-reaction only takes place in substrates that contain vicinal diol functionalities.

4.6 Summary

A procedure for the direct conversion of primary alcohols and aldehydes to form methyl esters has been developed in which oxygen is used as the stoichiometric oxidant. Gold nanoparticles have also been demonstrated to be highly active catalysts for the oxidation of aldehydes as this reaction can take place at temperatures as low as -78 ºC [109]. Furthermore, the oxidative esterification procedure has been applied for the valorization of HMF and glycerol leading to FDMC and dimethyl mesoxalate in high yields, thereby leading to new chemical building blocks from biomass [108, 110].

Experimental

All chemicals were purchased from commercial sources and used without further purification. 1 wt% Au/TiO_2 was acquired from the World Gold Council (Gold reference catalyst #02-06, Sued-Chemie Catalysts Japan). Methanol (99.9% pure, Sigma-Aldrich), 1-hexanol (98%, Riedel-de Haën), sodium methoxide solution (30 wt% in methanol, Sigma-Aldrich), cinnamyl alcohol (98%, Sigma-Aldrich), benzyl alcohol (>99%, Bie & Berntsen), 2-(hydroxymethyl) pyridine (98%, Aldrich) and oxygen (>99.6%, Strandmøllen). The autoclave used was a 325 ml titanium stabilized T316 autoclave, from the Parr Instrument Company. The GC used was an Agilient Technologies 6890N Network GC System equipped with a flame ionization detector (FID) and a DB-1 column (50 m x 0.320 mm, 5.00 micron, J&W Scientific, catalog 1231055). All NMR-spectra were recorded on a Varian Mercury 300 MHz instrument. Chemical shifts were correlated relative to chloroform. The data were processed with MestReC 4.7.4.0 software.

General experimental procedure

The autoclave was charged with Au/TiO_2, methanol, substrate, and the base additive (30 wt% sodium methoxide in methanol) was added with a pipette. A 3 cm magnetic stir bar was fitted in the autoclave which was then filled with dioxygen, giving an O_2/substrate ratio of 7:1. The autoclave was placed in a 130 °C preheated oil bath, and the reaction mixture was stirred rapidly. The autoclave was removed from the oil bath after the specified reaction time and was allowed to cool to room temperature. Analysis was done by centrifugation of ca. 1 mL of the reaction mixture and then analyzing the liquid by injecting 0.2 μL into the GC. Retention times of the products were verified by comparison to authentic samples.

Analysis of the gas-phase of the reaction mixture was done in the following way: The autoclave was charged with methanol (12.2 mL, 300 mmol), 1-hexanol (2.0 mL, 16 mmol), sodium methoxide in methanol (0.6 mL 30 wt%, 3 mmol) and 1 wt% Au/TiO_2 (0.50 g). A 3 cm magnetic stir bar was added, and the autoclave was filled with oxygen to a total pressure of 10 bar (9.2 bar of pure oxygen, ca. 115 mmol). The autoclave was placed on a 130 °C preheated oil bath under rapid stirring. 24 hours later, the autoclave was removed from the oil bath and cooled to room temperature. A plastic balloon with a vent was flushed 3 times with nitrogen and evacuated. The balloon was then filled with gas from the autoclave, and the gas was analyzed on a GC (Shimadzu GC-17A) with a thermal conductivity detector (TCD). A reference run with 2 mol% CO_2 was performed, and based on this reference experiment, the reaction gas was found to consist of 78 mol% CO_2.

Methyl hexanoate

The autoclave was charged with methanol (12.15 mL, 300 mmol), 1-hexanol (2.0 mL, 16 mmol), 30% sodium methoxide in methanol (60 μL, 0.32 mmol), 1 wt% Au/TiO_2 (0.50 g) and fitted with a magnetic stir bar. The autoclave was filled with oxygen to a total pressure of 10 bar (9.2 bar of pure oxygen, *ca.* 115 mmol). The autoclave was then placed in a 130 °C preheated oil bath under rapid stirring. After 10 hours, the autoclave was cooled to room temperature, and the reaction mixture was centrifuged. The clear liquid was transferred into a 100 mL separatory funnel with 50 mL of water and extracted twice with 25 ml of pentane. The combined pentane phases were washed with 25 ml of water and 25 mL of brine. The organic layer was then dried with magnesium sulphate, and the pentane was distilled off at 1 atm. The residue was transferred to a Kugelrohr-bulb and bulb-to-bulb distilled at 150 °C. Yield: 1.65 g (79%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.86 (t 3H), 1.19-1.36 (m, 4H), 1.51-1.65 (m, 2H), 2.26 (t, 2H), 3.63 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.81, 22.25, 24.57, 31.24, 33.98, 51.34, 174.25 ppm.

Methyl benzoate

The autoclave was charged with methanol (12.15 mL, 300 mmol), benzyl alcohol (1.65 mL, 16 mmol), 30% sodium methoxide in methanol (60 μL, 0.32 mmol), 1 wt% Au/TiO_2 (0.50 g) and fitted with a magnetic stir bar. The autoclave was filled with oxygen to a total pressure of 10 bar (9.2 bar of pure oxygen, *ca.* 115 mmol). The autoclave was then placed in a 130 °C preheated oil bath under rapid stirring. After 10 hours, the autoclave was cooled to room temperature, and the reaction mixture was centrifuged. The clear liquid was transferred into a 100 mL separatory funnel with 50 mL of water and extracted twice with 25 mL of pentane. The combined organic phases were washed with 25 mL of water and 25 mL of brine. The organic layer was then dried with magnesium sulphate, and the pentane was distilled off at 1 atm. The residue was transferred to a Kugelrohr-bulb and bulb-to-bulb distilled at 130-140 °C and 100 mm Hg. Yield: 1.74 g (79%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.90 (s 3H), 7.39-7.46 (m, 2H), 7.51-7.58 (m, 1H), 8.01-8.07 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 52.00, 128.25, 129.46, 130.02, 132.81, 166.99 ppm.

Methyl cinnamate

The autoclave was charged with methanol (12.15 mL, 300 mmol), cinnamyl alcohol (2.05 mL, 16 mmol), 30% sodium methoxide in methanol (60 μL, 0.32 mmol), 1 wt% Au/TiO_2 (0.50 g) and fitted with a magnetic stir bar. The autoclave was filled with oxygen to a total pressure of 10 bar (9.2 bar of pure oxygen, *ca.* 115 mmol). The autoclave was then placed in a 130 °C preheated oil bath under rapid stirring. After 10 hours, the autoclave was cooled to room temperature, and the reaction mixture was centrifuged. The clear liquid was transferred into a 100 mL separatory funnel with 50 mL of water and extracted twice with 25 ml of pentane. The combined organic phases were washed with 25 ml of water and 25 mL of brine. The organic layer was then dried with magnesium sulphate, and the pentane was removed on a

rotevaporator. The solid residue was dissolved in a small amount of heptane and flash chromatographed to remove methyl benzoate (3 cm in diameter column; eluent: heptane:ethyl acetate 19:1; rf: 0.2). Yield: 1.98 g (76%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.81 (s 3H), 6.45 (d, 1H, *J* = 16.26 Hz), 7.36-7.42 (m, 3H), 7.49-7.56 (m, 2H), 7.70 ppm (d, 1H, *J* = 16.26 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.70, 117.73, 128.03, 128.85, 130.27, 134.31, 144.84, 167.41 ppm.

Methyl pyridine-2-carboxylate

The autoclave was charged with methanol (12.15 mL, 300 mmol), 2-(hydroxymethyl) pyridine (1.55 mL, 16 mmol), 30% sodium methoxide in methanol (60 μL, 0.32 mmol), 1 wt% Au/TiO_2 (0.50 g) and fitted with a magnetic stir bar. The autoclave was filled with oxygen to a total pressure of 10 bar (9.2 bar of pure oxygen, *ca.* 115 mmol). The autoclave was then placed in a 130 °C preheated oil bath under rapid stirring. After 10 hours, the autoclave was cooled to room temperature, and the reaction mixture was centrifuged. The methanol and water were removed on the rotevaporator, and the brownish residue was distilled (95 °C and 3 mm Hg) to afford a colorless oil. Yield: 1.87 g (85%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.91-3.92 (m, 3H), 7.37-7.43 (m, 1H), 7.72-7.80 (m, 1H), 8.02-8.07 (m, 1H), 8.63-8.68 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 52.70, 124.92, 126.80, 136.88, 147.62, 149.58, 165.45 ppm.

Furan 2,5-dimethylcarboxylate

The autoclave was charged with 0.25 g of 1 wt% Au/TiO_2 (0.013 mmol Au), 12.65 mL of methanol (300 mmol), 0.50 g of HMF (4.0 mmol, >99%, SAFC), and 0.060 mL of 30 wt% sodium methoxide in methanol (0.3 mmol). The autoclave was fitted with a magnet stir bar, flushed with oxygen and pressurized with 4 bar O_2 (52 mmol). The autoclave was then heated in an oil bath at 130°C for the desired reaction time. After the reaction, the autoclave was cooled to room temperature and the reaction mixture was analyzed by dissolving all organic material with an excess of methanol and analyzing it by GC. FDMC was isolated by removal of methanol under reduced pressure. The remaining beige solid was sublimated at 1 atm and 160°C to afford colourless crystals (figure 4.7). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.92 (m, 6H), 7.21 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 52.39, 118.46, 146.57, 158.37 ppm.

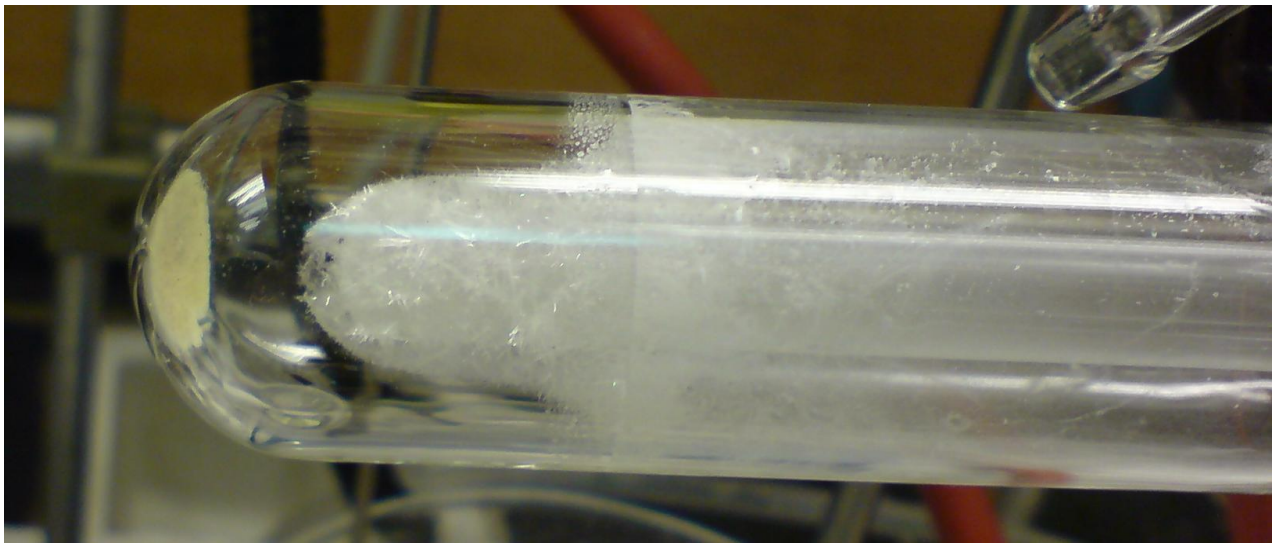


Figure 4.7 Sublimation of crude FDMC to afford colorless crystals of pure FDMC.

5-hydroxymethyl methylfuroate and methyl furoate

A two-necked 100 mL round bottomed flask was charged with 0.25 g of 1 wt% Au/TiO_2 (0.013 mmol Au), 12.65 mL of methanol (300 mmol), 0.50 g of HMF (4.0 mmol, >99%, SAFC) or 0.38 g of furfural (4.0 mmol, >98%, Fluka), and 0.060 mL of 30 wt% sodium methoxide in methanol (0.3 mmol). The flask was equipped with a rubber septum, and a condenser, and fitted with a magnetic stirrer bar. The flask was flushed with oxygen and kept under an oxygen atmosphere. The reaction mixture was then stirred vigorously (22 ºC) and samples of the reaction mixture were taken out with a syringe. The samples were then analyzed by GC and GCMS.

Oxidative esterification of aldehydes at ambient temperatures

A 25 ml round bottomed flask was charged with 10 ml methanol (247 mmol), 870 mg of benzaldehyde (8.2 mmol), 148 mg of a 30 wt% NaOMe solution in methanol (0.82 mmol NaOMe). Finally, 320 mg of 1 wt% Au/TiO_2 was added and the mixture was stirred at room temperature (22-25 ºC). The flask was fitted with a reflux condenser and a calcium chloride tube, to keep moisture out. For the experiments performed at -20 and -78 ºC, the flask was fitted with a rubber septum and a ballon with a large excess of air. Samples were acquired frequently using a syringe with a filter and analyzed by GC and compared to an authentic sample of methyl benzoate.

Acrolein was oxidized using slightly modified conditions. 168 mg of acrolein (3.0 mmol) was added to a 25 mL round bottomed flask containing 10 mL methanol (247 mmol). Then 500 mg of Au/ZnO (supplied by Mintek) was added and the flask was fitted with a calcium chloride tube and stirred for 40 hours. Samples were acquired, analyzed by GC and compared with an authentic sample of methyl acrylate.

Oxidative esterification of glycerol and diols

Glycerol (>99%) from H. Struers Chemical Labs, methanol (>99.9%), 30 wt% sodium methoxide in methanol, 1,2-propanediol (>99%) and 1,3-propanediol (>99%), anisol (>99%), 1-hydroxyacetone (90%), methyl lactate (99%), methyl pyruvate (95%), methyl acrylate (>99%), and dimethyl malonate (>99%) were all aquired from Sigma-Aldrich. Technical air (20% O_2, 80% N_2) was from Air Liquide. Gold catalysts, Au/TiO_2, Au/Fe_2O_3, were supplied by the World Gold Council [111].

The oxidation experiments are performed in a 50 mL steel autoclave (MicroClave from Autoclave Engineers). The autoclave is charged with 250 mg glycerol (2.7 mmol) and 5.1 g of methanol (159 mmol). 50 mg of a 30 wt% $NaOCH_3$ in methanol is added (0.27 mmol) together with 30 mg of anisol (0.28 mmol, internal standard). Then the 1% Au/TiO_2 catalyst is added (0.48 g, 0.024 mmol Au) and the autoclave is sealed and pressurized to 21 bar with technical air (*ca*. 8 mmol O_2). The mixture is stirred (900 rpm) and heated to 373 K. At regular intervals, the autoclave is cooled to 263 K, and a sample is taken out. The autoclave is then recharged with technical air, and reheated to 373 K. In this way, the time-dependencies of the oxidation of the polyols are mapped by plotting the concentrations of reactants and products to establish possible reaction routes. Oxidations of 1,2-propanediol and 1,3-propanediol are performed analagously, by using 210 mg of each, corresponding to 2.7 mmol. Furthermore, oxidation of 1,2-propanediol is performed by using 0.96 g of 1% Au/TiO_2 catalyst.

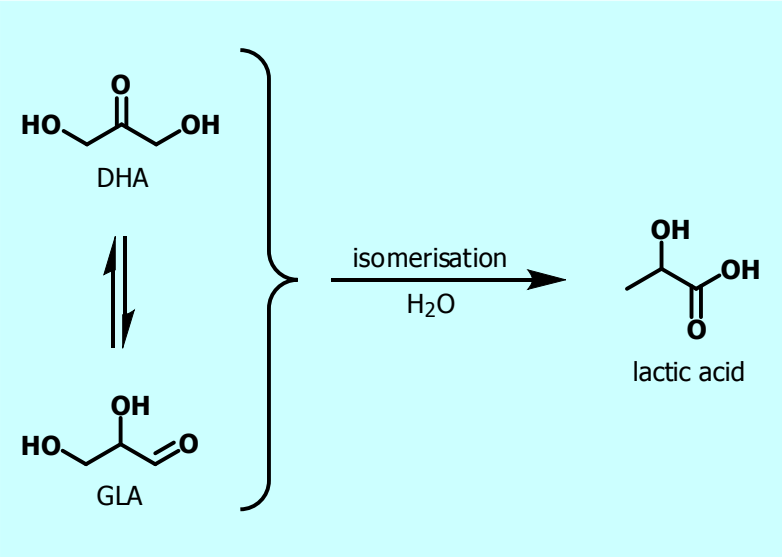
The reaction mixtures were analyzed by GC (Agilent Technologies 6890N, column was an HP-5 from J & W Scientific, 30 m long and a diameter of 0.32 mm, and has an inner film of 0.25 μm 5% methyl phenyl siloxane) and GC-MS (Shimadzu Spectachrom QP5000 GC-MS, column was Supelco Equity-1 of 30 m in length, inner diameter of 0.25 mm and an inner film of dimethyl polysiloxane). Reference samples were used to confirm the products whenever possible. However, the oxidation products dimethyl tartronate and methyl-3-hydroxypropionate could not be obtained and identification was thus conducted on the basis on MS-data: Methyl glycerate was generated *in situ* by dissolving sodium glycerate (>99% from Sigma-Aldrich) in methanol and adding a small excess of 18M sulphuric acid and heating to 60 °C for one hour. Dimethyl mesoxalate is not commercially available. However dissolving commercially available diethyl mesoxalate (>95%, Sigma-Aldrich) in methanol in the presence of base affords dimethyl mesoxalate and ethanol. On basis of these procedures it was possible to acquire reference data of the retention times of methyl glycerate and dimethyl mesoxalate. Quantifiable product data was obtained from GC. The concentration change due to methanol consumption in the oxidative esterification is ignored in the calculation of product concentrations.

[†]Contribution to this work

Most of the experimental work in this chapter was carried out by then undergraduate students Inger S. Nielsen and Anders T. Madsen. My contribution to this work has primarily involved design of the experiments and supervision of the undergraduate students as well as analysis of GC and GC-MS chromatograms and mass spectra. I also isolated the products in the cases where this was done.

5. Production of Lactic Acid and Lactate Esters from Biomass

The goal of this project is to develop an efficient procedure in which the triose sugars dihydroxyacetone (DHA) and glyceraldehyde (GLA) can be converted into lactic acid in water and lactate esters in alcohols, using a heterogeneous catalyst (scheme 5.1).



Scheme 5.1

This transformation may seem obscure, but it is merely an isomerisation reaction that is thermodynamically highly favorable. The relative stability of the three isomers is in the order of lactic acid >> DHA > GLA. The triose sugars can be formed by aerobic oxidation of glycerol using a charcoal supported platinum-bismuth catalyst in high yields [47-48] or by fermentation of glycerol using the *gluconobactor suboxydans* strain [112]. This isomerisation reaction could thus be envisioned as a new route to lactic acid from biomass that does not involve fermentation of glucose, but instead partial oxidation of glycerol to form DHA or GLA followed by an isomerisation step.

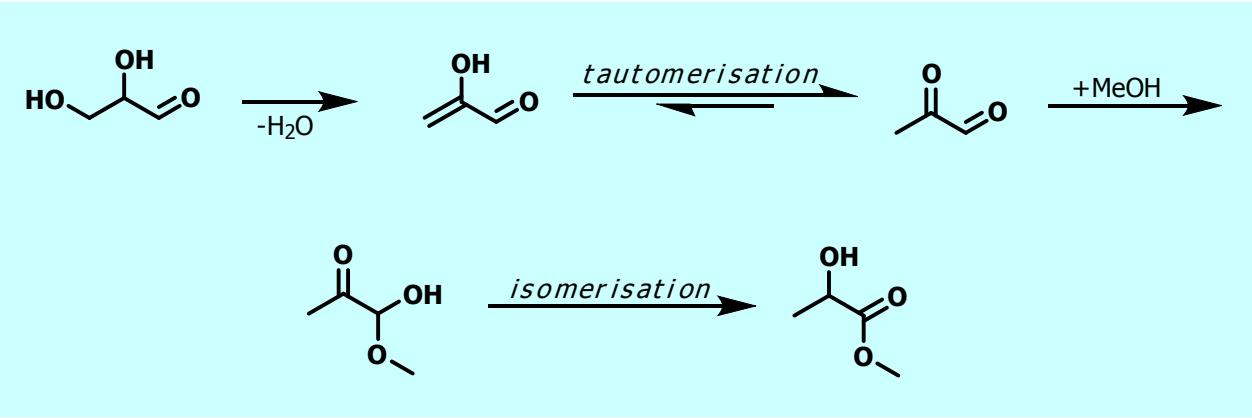
5.1 Lactic acid

Lactic acid is an important chemical that is used in many food-related applications and cosmetic products. More interestingly is though that lactic acid can be polymerized to form poly(lactic acid) (PLA), which is a biodegradable thermoplastic that has a the potential to replace petroleum derived plastics in applications such as food wrapping, drinking bottles, clothing and many other places. However, despite of its many desirable properties, the high cost has impeded a more widespread implementation of PLA.

The largest producer of lactic acid is NatureWorks LLC, located in the corn-belt in the United States, with a production capacity of 150.000 tons annually [39]. Currently L(+)-lactic acid is obtained by fermentation of glucose under anaerobic conditions using various *Lactobacillus* strains [113-114]. Although high yields of lactic acid can be produced in this way using glucose as a cheap feedstock, the overall process has some inherent disadvantages which add to the cost of lactic acid. One disadvantage is the fact that the fermentation process typically takes 2-4 days and is performed batch-wise. Another disadvantage is related to the inability of the bacterial strains to function under an acidic environment. This requires that the lactic acid must be neutralized as it is formed, with the use of a stoichiometric amount of base (typically calcium hydroxide). Purification of the crude calcium lactate is done by recrystallisation and acidification with sulphuric acid to form crude lactic acid and an almost equal weight amount of gypsum. Final purification is achieved by esterification with methanol to form methyl lactate, distillation and hydrolysis to release the pure L(+)-lactic acid.

5.2 Background for triose isomerisation

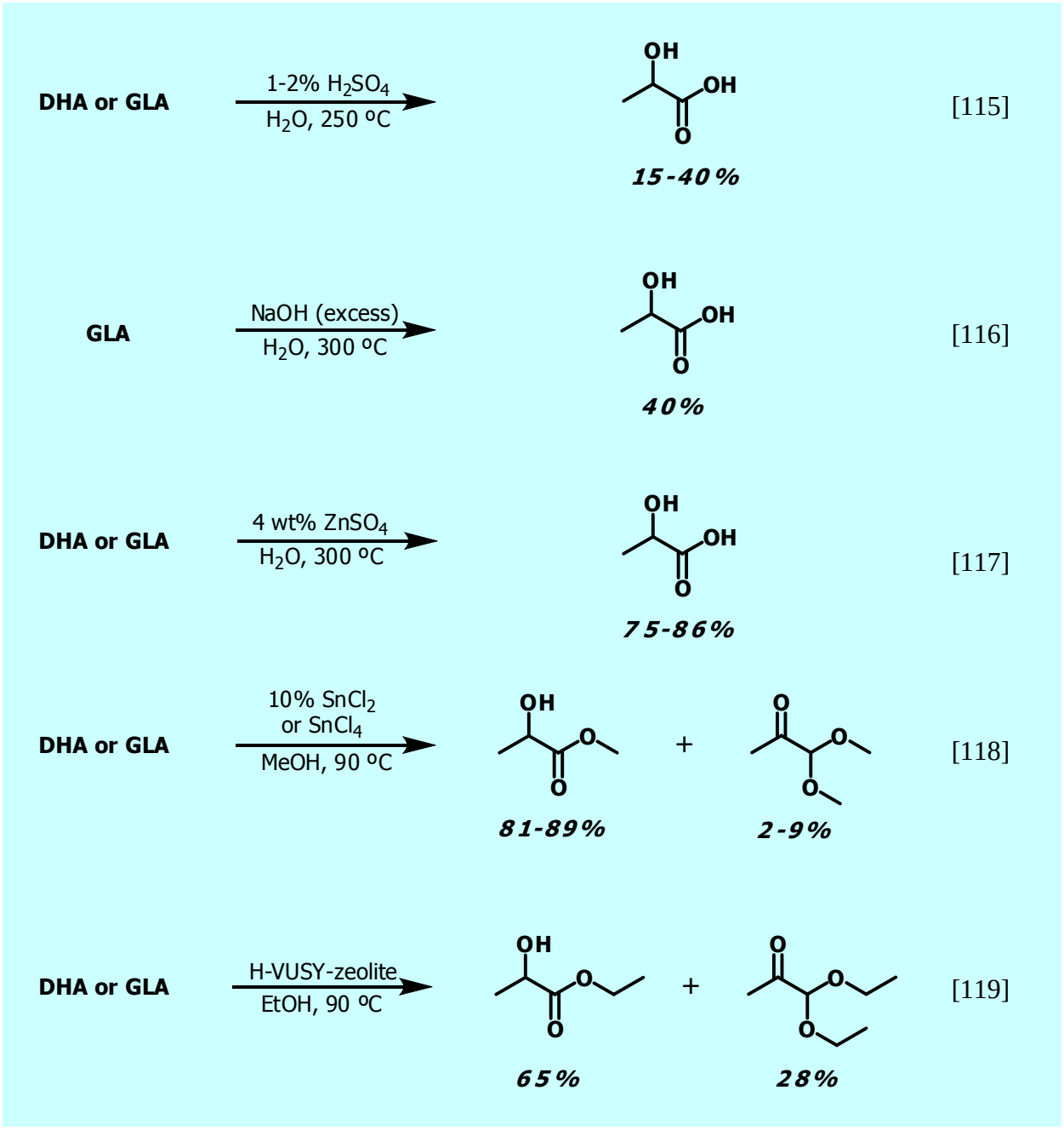
Isomerisation of DHA and GLA to lactic acid has been reported to take place in water, using homogeneous catalysts such as sulphuric acid [115], sodium hydroxide [116] and zinc sulphate [117]. Some reports have also been made in which the isomerisation reaction is performed in alcohol solvents (scheme 5.3).



Scheme 5.2

When an alcohol is used as solvent, the product becomes the corresponding methyl lactate ester instead of lactic acid. Sasaki *et al.* have used tin chloride in methanol to form methyl lactate in good yields [118] and Jacobs have used steam-dealuminated H-Y zeolites (H-VUSY) in ethanol to transform DHA to ethyl lactate in moderate yields [119]. In some cases, pyruvaldehyde dialkyl acetal is formed along side the lactate ester. Sasaki has suggested a plausible reaction pathway for

the formation of methyl lactate that involves dehydration of DHA/GLA to form pyruvaldehyde as an intermediate. Addition of methanol to pyruvaldehyde will form a hemiacetal intermediate which followed by 1,2-hydride shift will then lead to methyl lactate (scheme 5.2). Although this reaction pathway explains the formation of methyl lactate, it does not explain why pyruvaldehyde dimethyl acetal is formed in some cases.



Scheme 5.3

5.3 Zeolites

Zeolites are crystalline materials made up by $[SiO_4]^{4-}$ and $[AlO_4]^{5-}$ tetrahedra to form well defined structures containing micropore channels and cavities [120]. Depending on the preparation procedure, various types of zeolites with different microporous systems can be synthesized (three relevant framework structures are given in figure 5.1).

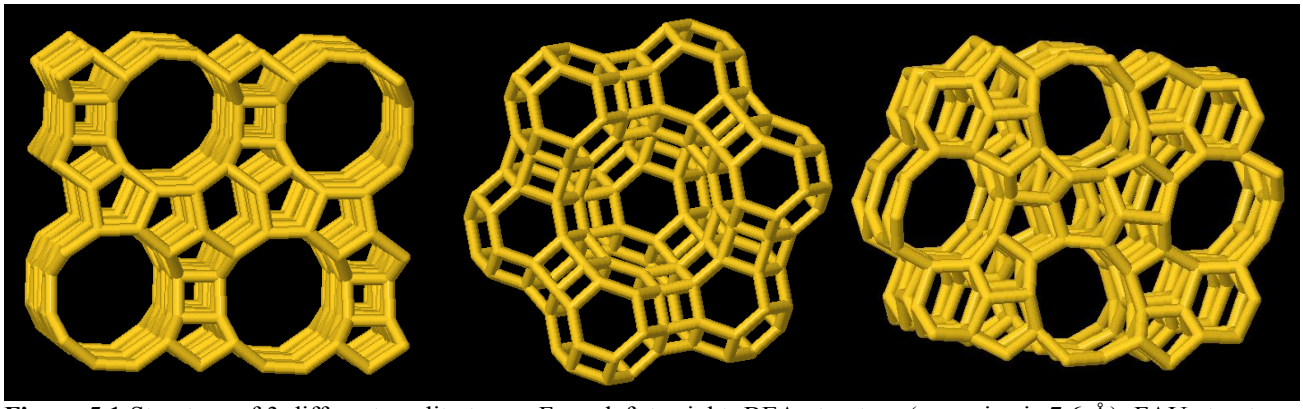


Figure 5.1 Structure of 3 different zeolite types. From left to right: BEA-structure (pore-size is 7.6 Å), FAU-structure (family of Y, pore-size is 7.8 Å) and MFI-structure (family of ZSM-5, pore-size is 5.5Å) [119].

One of the key abilities of zeolites is their high thermal stability (up to 5-600 ºC) and large surface area due to their micropore channels and cavities. The dimension of these channels is in the size region of simple molecules, and therefore zeolites can be used for shape-selective catalysis and as molecular sieves. The acidity of a zeolite can be fine-tuned and is possible to make both hydrophobic and hydrophilic zeolites. The acidic properties of a zeolite is proportional to the amount of aluminum present (Si:Al ratio) because aluminum has to be charge compensated with a cation when it is built into the zeolite framework in place of silicon. For this reason, zeolites are often termed “solid acids” and are used extensively as industrial catalysts in oil refining. Aluminum can also be present in zeolites as octahedral aluminum which is the case when it is not built tetrahedrally into the zeolite framework. Here, aluminum is not charge compensated with a cation and different zeolite properties can be achieved. Typically extra-framework aluminum will have Lewis acidic properties in contrast to Brønsted acidity in the framework. Framework aluminum can be transformed into extra-framework aluminum by de-alumination where the zeolite is *e.g.* treated with steam at very high temperatures. It is noteworthy to mention that the de-alumination process does not change the Si:Al ratio of the material. Many different variants of the steam de-alumination process exist, and different terminologies such as “ultra stable” and “super de-aluminated ultra stable” are used to differentiate between the methods used in the de-alumination process. There are many ways to design zeolites by using different zeolite templating agents, changing the aluminum

content and the aluminum form and even incorporating tetravalent metal ions into the zeolitic structure to achieve different material properties.

The remaining part of this chapter describes the development of an isomerisation-esterification procedure that enables complete product selectivity, ranging from full selectivity to methyl lactate to full selectivity to pyruvaldehyde dimethyl acetal using different solid catalysts.

5.4 Results and discussion[†]

Unaware of the work of Jacobs using acidic Y zeolites to catalyze the isomerisation reaction in ethanol [119], we investigated the use of similar zeolites in methanol and water. A commercial catalyst series from Zeolyst International [121] was screened for the isomerisation reaction using both methanol and water as solvent and then analyzed by GC and HPLC, respectively. Here, various zeolites such as H-BEA, H-ZSM-5 and H-mordenite and steam-dealuminated H-Y were tested as well as the effect of altering the Si:Al molar ratio was examined (table 5.1). The isomerisation reactions were carried out in a small pressure resistant glass vial at 115 ºC in methanol and 125 ºC in water.

Zeolite	Si:Al ratio	Lactic acid yield (%)[d]		Methyl lactate yield (%)[e]	
		DHA	*GLA*	*DHA*	*GLA*
H-VUSY[a]	6	71	63	96 (3)	98 (2)
H-SDUSY[b]	30	47	41	26 (53)	25 (39)
H-BEA	12.5	63	60	42 (46)	63 (27)
H-BEA	19	37	37	10 (69)	8 (56)
H-ZSM-5	11.5	32	30	17 (58)	19 (54)
H-ZSM-5	25	22	23	7 (55)	7 (52)
H-Mor	10	39	32	8 (67)	10 (18)
No catalyst	-	3	4	0	0
Acidic resin[c]	-	11	-	0 (78)	-

Table 5.1 80 mg catalyst, 1.25 mmol substrate (calculated as monomer), 4 g solvent (water or methanol) are used, for the experiments in methanol, naphthalene is used as internal standard. Reaction time is 24 hours except for reaction with GLA in methanol where it is 48 hours. Reaction temperature is 115 °C in methanol and 125 °C in water. a) Very Ultra Stable Y (Y-zeolite calcined with steam in the ammonium-form) b) Super Dealuminated Ultra Stable Y (Y-zeolite calcined with steam in the proton-form) c) DOWEX® 50WX8-100 d) HPLC-yield e) GC-yield. Yield in parenthesis is the GC-yield of PADA.

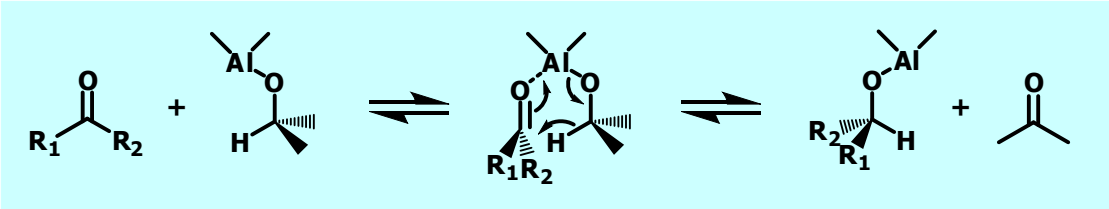
As it turns out, the catalytic activity and the product selectivity of the various zeolites are very different. A simplified reactivity trend is that the highly aluminous zeolites (low Si:Al ratios) give high yields of methyl lactate and lactic acid, whereas the zeolites only containing small amounts of aluminum leads to high yields of pyruvaldehyde dimethyl acetal (PADA) in methanol. In general, the yields are better in methanol than in water, where product loss is primarily caused by the formation of carbonaceous deposits that was visible as a darkening of the reaction mixture. When

the reaction is performed in methanol the reaction mixture remains almost colorless, indicating a more selective reaction. The most active catalyst H-VUSY (6) is capable of forming methyl lactate in almost quantitative yields, which is considerable better than any other procedure reported so far. Furthermore there does not seem to be any significant difference in the product selectivity when using either DHA or GLA as substrate. HPLC analysis of the reaction mixture at intermediate times also shows that DHA and GLA in equilibrium during the reaction. An experiment where pyruvaldehyde is used as substrate in water led to the formation of lactic acid in 73% yield, indicating that this is a likely intermediate in the reaction (pyruvaldehyde can be considered a triose anhydride) and that the reaction therefore could be taking place in the fashion that Sasaki suggests. However, when PADA is used as substrate, only trace amounts of methyl lactate forms, indicating that PADA does not convert to the hemiacetal readily, even if small amounts of water are added.

5.5 Importance of acidity

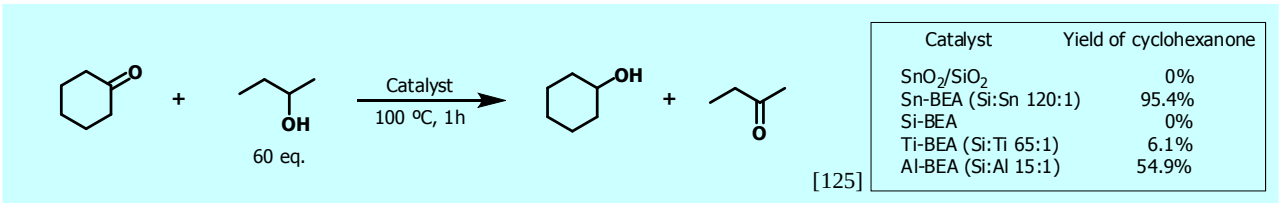
As mentioned, high yields of PADA are formed for some catalysts when the reaction is performed in methanol. When *e.g.* using H-ZSM-5 with a Si:Al ratio of 11.5, PADA is the major product being formed in more than 50% yield. More interestingly, when an acidic ion exchange resin is used instead of a zeolite PADA is formed in a 78% yield. The most active catalyst for the formation of methyl lactate and lactic acid is the steam-dealuminated H-VUSY (6) zeolite. This particular zeolite is steam de-aluminated, which means that a large amount of the aluminum is present as the Lewis acidic extra-framework aluminum. In contrast to this, the acidic ion exchange resin only contains Brønsted acidity. It therefore seems likely that the difference in product selectivity for the various catalysts is caused by a difference in the acidities of the catalysts.

The reaction pathway proposed by Sasaki is a dehydration reaction followed by addition of methanol and finally a redox step. The catalyst therefore has to be capable of catalyzing a dehydration reaction as well as a redox reaction in order to form methyl lactate. Most Brønsted and Lewis acidic catalysts are capable of catalyzing dehydration reactions. The dehydration of fructose to HMF is, for example, known to proceed using both aqueous HCl as well as Lewis acidic metal chlorides [28, 30]. Not every catalyst can catalyze redox reactions, though. In this case, the final redox step (scheme 5.2) bears a distant resemblance to the Meerwein-Ponndorf-Verley reduction and Oppenauer oxidation (MPVO-redox) in which an alcohol is oxidized by a ketone or an aldehyde under the influence of a Lewis acidic catalyst (Scheme 5.4).



Scheme 5.4

The MPVO-redox reaction has found some use in organic chemistry, particularly in the first half of the 20th century, with aluminum isopropoxide and aluminum *tert*-butoxide being the most commonly used catalysts [122]. These aluminum alcoxides function as soluble Lewis acids. However, in recent years heterogeneous MPVO-catalysts have also been reported [123-125]. The most notable reports in this field are made by Avelino Corma and co-workers, who have incorporated tin into the framework of the BEA zeolite to make a Sn-BEA catalyst that is highly active for the MPVO-redox reaction [125]. Indeed, this catalyst is much more active and selective than the corresponding conventional Al-BEA zeolite (Scheme 5.5).



Catalyst	Yield of cyclohexanone
SnO_2/SiO_2	0%
Sn-BEA (Si:Sn 120:1)	95.4%
Si-BEA	0%
Ti-BEA (Si:Ti 65:1)	6.1%
Al-BEA (Si:Al 15:1)	54.9%

Scheme 5.5

We therefore decided to synthesize this particular zeolite according to the procedure reported by Corma [126] in order to test its activity for the rearrangement of dihydroxyacetone to lactic acid and methyl lactate in water and methanol, respectively.

5.6 Isomerisation using Lewis acidic zeolites

In addition to making the Sn-BEA zeolite we made Al-BEA, Zr-BEA, Ti-BEA with similar silicon:metal ratios, as well as pure Si-BEA for comparison. Deposition of metal-precursors to make SnO_2, Al_2O_3 and ZrO_2 deposited on the pure Si-BEA zeolite using incipient wetness impregnation was also made for comparison. This would enable a thorough study of the effect of the particular metal as well as the effect of incorporating a metal into the framework of the zeolite or depositing it as the metal oxide in the zeolite pores. We conducted a similar series of experiments as we had done for the conventional acidic zeolites (table 5.2).

It was quickly discovered that the Sn-BEA catalyst was far more active that the previously used H-VUSY (6) zeolite. Therefore the temperature was lowered to 80 ºC for the reactions performed in

methanol. Under these conditions full conversion of DHA was achieved after 24 hours while maintaining a very high yield of methyl lactate. The corresponding H-VUSY (6) zeolite only gives 65% methyl lactate after 24 hours at these conditions. This corresponds to a TON for each tin-atom of 118 as compared to 4.3 for aluminum in H-VUSY. The Sn-BEA also gives higher yields of lactic acid (90%) for the isomerisation reaction when it is performed in water than the conventional zeolite does (71%). It was possible to reuse the Sn-BEA catalyst in methanol for 3 consecutive runs without any noticeable loss in activity, by simply adding fresh DHA after the 24 hours reaction. However in water this was not possible as large amounts of carbonaceous deposits were formed, resulting in a decrease in the formation of lactic acid from 90% after first run to 21% after second run. This could be a result of the unavoidable presence of Brønsted acid in the aqueous reaction mixture, as the concentration of lactic acid increase.

Catalyst	Yield of methyl lactate (%)[b]	Yield of lactic acid (%)[c]
Al-BEA	0	22
Al_2O_3/BEA	0	8
Zr-BEA	1	44
ZrO_2/BEA	0	13
Sn-BEA	>99	90
Sn-BEA[d]	>99	90
SnO_2/BEA	<1	8
Ti-BEA	2	25
Si-BEA	0	3
Acidic resin	<1	11
No catalyst	0	3

Table 5.2 1,25 mmol DHA in 4 g of methanol or water, 80 mg catalyst is added and the mixture is stirred for 24 hours. Si:Me is 125:1 in all cases, except for Al-BEA where it is 65:1. [b]Reaction temperature is 80 °C yield is based on GC using an internal standard. [c]Reaction temperature is 125 °C, yield is based on HPLC. [d]GLA used as substrate.

An interesting observation is that when tin is incorporated into the zeolite framework it becomes more active than homogeneous tin in the form of $SnCl_4 \cdot 5H_2O$. Thus, the TOF for the formation of methyl lactate using Sn-Beta is 60 per tin-atom in the first hour whereas it was only 24 using a similar amount of $SnCl_4 \cdot 5H_2O$ as the molar amount of tin in the Sn-Beta catalyst. Additionally, SnO_2/Si-Beta was found to give only trace amounts of methyl lactate although the material contains the same amount of tin as the Sn-Beta zeolite. This effect of framework incorporation has also been reported by Corma [125]. Corma furthermore reports that in a zeolite synthesized according his procedure, only tetrahedral tin is seen in ^{119}Sn-NMR and no octahedrally coordinated species are present.

Obviously incorporation of tin results in a much more active and selective isomerisation catalyst than incorporation of other metals. The Lewis acid strength of the metal site in the zeolite framework can be evaluated by its ability to shift the carbonyl stretching frequency of

cyclohexanone in IR. Such IR-measurements were performed on the Sn-BEA, Ti-BEA and Zr-BEA catalysts. Here it was found that the cyclohexanone C=O stretch shifts by 49 cm^{-1} for Sn-BEA, 29 cm^{-1} for Zr-BEA and 22 cm^{-1} for Ti-BEA. These results thus indicate that Sn-BEA contains much stronger Lewis acid sites than Zr-BEA and Ti-BEA, which could explain its increased catalytic activity.

Interestingly Sn-BEA, Zr-BEA and Ti-BEA do not form any PADA. In order to fully study the selectivity of the various catalysts for the formation of methyl lactate and PADA, a reaction series was performed at a higher temperature (115 ºC), where the other catalysts are also appreciably active. The yields of methyl lactate and PADA when using the different catalysts are shown in figure 5.2. Here it is seen that the acidic ion exchange resin is highly selective towards the formation of PADA whereas Sn-BEA, Zr-BEA and Ti-BEA are only selective for the formation of methyl lactate. Al-BEA is selective towards both products but is more selective for the formation PADA, suggesting that it largely contains framework aluminum that is Brønsted acidic. In order to substantiate this argument, we decided to steam-dealuminate the Al-BEA zeolite for comparison.

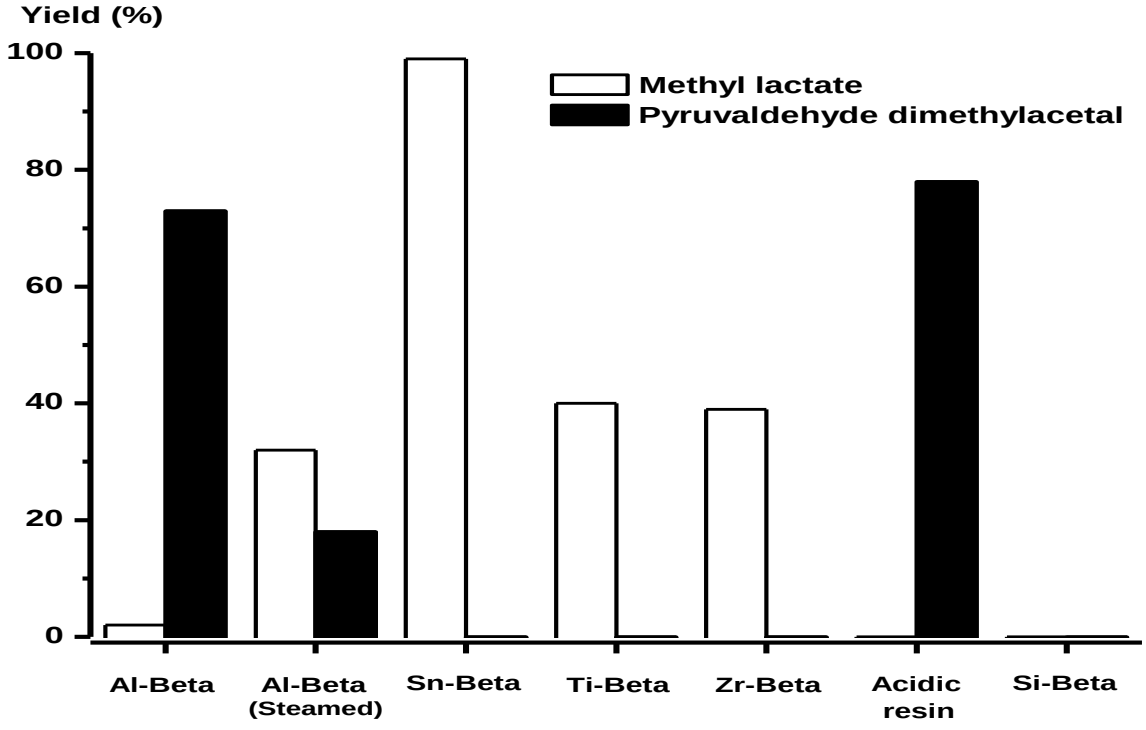
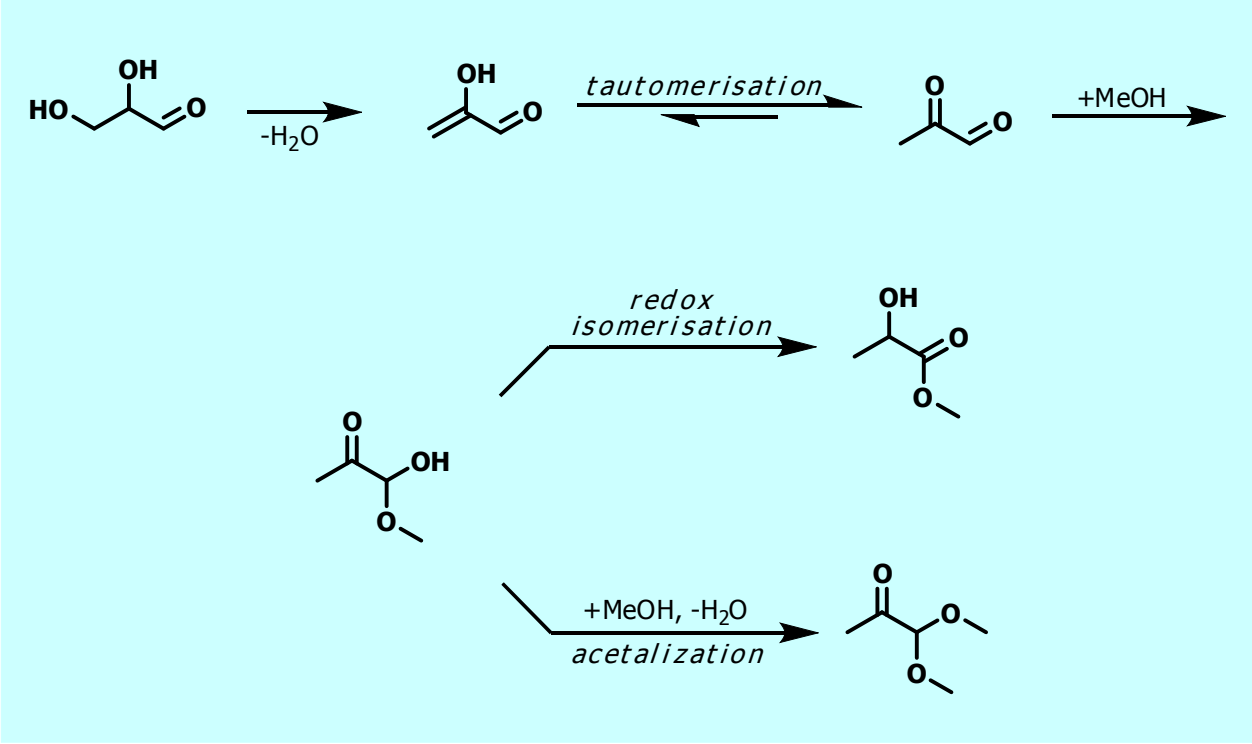


Figure 5.2 Yield of methyl lactate and PADA for the various Lewis and Brønsted acidic catalysts. Conditions: DHA (1.25 mmol) dissolved in 4 g of methanol was stirred with 80 mg of catalyst at 115 ºC for 24 hours. The yields are determined by GC.

Hence, the Al-BEA was heated in an argon-steam stream at 750 ºC for 20 hours. Here it was found, as expected from the selectivity of H-VUSY (6), that the steam-treatment shifts the selectivity towards the formation of methyl lactate instead of PADA as more extra-framework aluminum becomes present. Indeed the selectivity shift is so large that methyl lactate formation is favored over PADA formation. Steam-treatment at 550 ºC and 650 ºC resulted in a similar trend, although the effect was much less pronounced. This difference in selectivity for the catalysts can then likely be attributed to their relative differences in Lewis and Brønsted acidity.



Scheme 5.6

Sn-BEA, Zr-BEA and Ti-BEA are only Lewis acidic, whereas the acidic ion exchange resin is only Brønsted acidic. The Lewis acidic zeolites are capable of catalyzing a MPVO-type redox reaction of the hemiacetal intermediate, whereas pure Brønsted catalysts are not. Instead pure Brønsted catalysts will catalyze the formation of the acetal from the hemiacetal. It is now possible to draw a full reaction pathway for the isomerisation of DHA and GLA to methyl lactate and PADA, where the final step depends on which catalyst is used (scheme 5.6).

5.7 Summary

A more efficient procedure that works under milder conditions than any method reported so far for the isomerisation of triose sugars to methyl lactate and lactic acid has been developed. The reaction pathway that has been proposed by Sasaki [118] is supported by this work, and has been elaborated in order to explain the formation of PADA versus methyl lactate. This new knowledge could be valuable in the development of new catalysts in this field. Furthermore, with the use of the pure Lewis acidic Sn-BEA zeolite it is possible to convert glycerol to lactic acid in a process that involves oxidation of glycerol to DHA or GLA and isomerisation under mild conditions.

Experimental

GC-analysis was performed on an Agilent 6890N instrument with an FID-detector. The column equipped was an HP-5 capillary column (30m length, 0.32mm internal diameter). A GC-MS instrument (Agilent 6850 GC system coupled with an Agilent 5975C mass detector) was also used in some cases for qualitative purposes. HPLC analysis was performed using an Agilent 1200 series instrument equipped with an Aminex® HPX-87H column (30 cm length). The eluent used was in all cases a 0.005 M aqueous sulfuric acid solution.

Chemicals used

Dihydroxyacetone dimer (97%, Aldrich), DL-glyceraldehyde (minimum 95%, Aldrich), pyruvaldehyde (40 wt% in water, SAFC), naphthalene (99+%, Aldrich), DOWEX® 50WX8-100 ion exchange resin (Aldrich) and methanol (Biotech grade, 99.93%, Aldrich) were all used as received from the chemical companies. Commercial samples of methyl DL-lactate (≥97%, Aldrich), L-(+)-lactic acid (98%, Aldrich) and pyruvaldehyde dimethylacetal (≥97%, Fluka) were used as reference compounds for GC and HPLC analysis.

Commercial catalysts from Zeolyst International

The zeolites, FAU, MFI, BEA and MOR with different silicon to aluminum ratios were purchased from Zeolyst international, USA. All the zeolites were received in the ammonium form, except H-SDUSY (30) which was already in the proton form. It was not possible to obtain the exact post-treatment procedure used in the synthesis of the Y-zeolites. The ammonium exchanged zeolites were calcined at 550 °C for 6h to remove ammonia and give the corresponding H-zeolites. Table 5.3 shows the surface area provided by Zeolyst International as well as the number of acid sites, which is calculated on basis of the reported Si/Al ratio of the zeolites.

Zeolite	Trade name	Si/Al ratio	Surface area (m^2/g)	Acid sites (μ mol/g)
H-VUSY	CBV 712	6	730	2363
H-SDUSY	CBV 760	30	730	528
H-BEA	CP 814E	12.5	680	1224
	CP814C	19	710	823
H-ZSM-5	CBV 2314	11.5	425	1498
	CBV 5524G	25	425	624
H-MOR	CBV 21A	10	500	1488

Table 5.3 Surface area and number of acidic sites in the commercial zeolites used.

Preparation of BEA catalysts

The BEA catalysts were all synthesized according to known literature procedures in a fluoride media [126-128]. BET-surface area and micropore volume was measured by nitrogen-sorption using a Micromeritics ASAP 2020 instrument. XRD-spectra were recorded on a Bruker AXS powder diffractometer and show that all catalysts are highly crystalline and have BEA structure. The expected micropore volumes (0.19-0.20 ml/g) also indicate that all materials are highly crystalline and have BEA structure. IR-measurements of cyclohexanone adsorption on the different materials were recorded by dosing consecutive aliquots of cyclohexanone vapours onto the material and recording the FT-IR spectra on a BioRad FTS 80 spectrometer. Al-BEA was steam-

Zeolite	Si/Me ratio	Micropore Volume (ml/g)	Surface area (m^2/g)
Si-BEA	-	0.19	462
Sn-BEA	125	0.19	478
Al-BEA	65	0.19	449
Ti-BEA	125	0.20	492
Zr-BEA	125	0.20	506

Table 5.4 Surface area and micropore volumes of the different BEA zeolites prepared in our lab.

dealuminated at 550 ºC, 650 ºC and 750 ºC for 20 hours in a flow of argon that has been bubbling through a water flask at room temperature in order to introduce steam.

Experimental procedure for the triose isomerisation

The triose (112.5 mg, 1.25 mmol) was added to a 15 ml Ace-vial together with 4 g of solvent (H_2O or MeOH) and naphthalene (*ca*. 60 mg, internal standard only for MeOH as solvent). Finally, 80 mg of catalyst was added and the flask was sealed with the Teflon lid and immersed into a preheated oil bath (80 or 120 ºC for MeOH and 140 ºC for H_2O). The internal reaction temperature was measured in a separate control experiment by drilling a hole in the Teflon cap and tightly inserting a thermocouple. This showed that the internal temperature for the experiments with methanol was 115 ºC and 125 ºC when water was used. After the desired reaction time, the flask was cooled to room temperature and a sample was acquired using a syringe with a filter. The sample was then analyzed by GC (MeOH, using internal standard) or HPLC (for H_2O as solvent, using a calibration curve).

[†]Contribution to this work

My contribution to this work includes getting the idea to investigate this particular reaction, performing the initial reactions using acidic catalysts and demonstrating that a quantitative yield of methyl lactate could be achieved using this approach. Based on the work using conventional acidic zeolites (much of this work was carried out by post doc. S. Saravanamurugan) I hypothesized that Lewis acidic zeolites would be highly active catalysts for the formation of methyl lactate. Ph.d-student Martin S. Holm synthesized and characterized the Lewis acidic zeolites. Experimental work using the Lewis acidic zeolites was carried out by me and S. Saravanamurugan.

6. Summary

In closing, I want to remind the reader of the need for green and sustainable chemistry. As I mentioned in chapter 1, the background for this relates to the limited resources that we have available, the long-term impact that human activity has on the global climate and the more short-term impact that our activity has on the environment. In my thesis I have given three examples of areas where chemistry can play a positive role in facing these challenges.

The Diels-Alder decarbonylation reaction is an example where the combination of two known reactions leads to a synergistic result, enables new synthesis possibilities, while at the same time forms less waste than previous methods.

The important properties of new materials such as gold nanoparticles have been demonstrated by their ability to make use of oxygen as a stoichiometric oxidant in the conversion of alcohols and aldehydes. This could make the phasing out of highly polluting oxidants one step closer. Additionally, gold nanoparticles have been used for the conversion of renewable building blocks into more interesting chemical building blocks, hereby demonstrating new ways to make use of the limited biomass.

The final example I have given is the development of a procedure to convert triose sugars into lactic acid in a non-fermentive way. This procedure could open up a new door in the area of biomass conversion. This example also shows the importance of choosing the right catalyst for a particular reaction.

Although these three examples will not in any way solve the major challenges we face, they are each examples of small improvements in the field of green and sustainable chemistry. They all have the common feature that they involve catalysis, and although catalysis plays a very important role in chemistry today, it is likely that future developments in the field of chemistry will depend even more on the use of catalysis.

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DOI: 10.1002/cssc.200700168

The Renewable Chemicals Industry

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The possibilities for establishing a renewable chemicals industry featuring renewable resources as the dominant feedstock rather than fossil resources are discussed in this Concept. Such use of biomass can potentially be interesting from both an economical and ecological perspective. Simple and educational tools are introduced to allow initial estimates of which chemical processes could be viable. Specifically, fossil and renewables value chains are used to indicate where renewable feedstocks can be optimally valorized. Additionally, C factors are introduced that specify the amount of CO_2 produced per kilogram of desired product to illustrate in which processes the use of renewable resources lead to the most substantial reduction of CO_2 emissions. The steps towards a renewable chemicals industry will most likely involve intimate integration of biocatalytic and conventional catalytic processes to arrive at cost-competitive and environmentally friendly processes.

Introduction

Currently, there exists an intense focus on the production of transportation fuels from biomass.[1–4] This focus can be attributed to a desire to significantly lower the emission of greenhouse gases, thereby minimizing global warming, and also to relinquish our dependence on fossil fuels. Moreover, biomass is the only accessible non-fossil source of carbon that can be processed into liquids that are easily incorporated into the existing transportation fuel infrastructure. In particular, the widespread use of bioethanol and biodiesel as fuel additives is rapidly gaining importance in many parts of the world, and significant efforts are now being devoted to develop technologies that are simultaneously more sustainable than current technologies and allow more efficient use of the available bioresources.

In some regions, it appears that bioethanol can indeed already be produced to be cost-competitive with gasoline.[5] However, it also seems that the extensive use of biomass to produce biofuels remains controversial from both an economical and an ecological perspective, and these issues clearly need to be resolved in a fully transparent manner. It is interesting that despite the ongoing efforts to widely introduce biofuels as fuel additives, all prognoses still predict the demand for fossil fuels to increase over the next decades.[6] Consequently, it is clear that there is a strong need to consider if there are other options for substituting fossil resources with bioresources.

Today, about 85% of all crude oil consumed is used for the production of transportation fuels,[6] and this is undoubtedly the reason that the production of biofuels attracts most attention when considering renewable alternatives. However, as much as 10% of crude oil is currently used for the production of industrial chemicals.[6,7] In general terms, these chemicals are significantly more economically valuable than transportation fuels and, simultaneously, their production often also involves the co-production of significant amounts of carbon dioxide. Taking this into account, it is conspicuous that relatively little attention has been given to develop the use of biomass as a raw material for the production of industrial chemicals.[8]

Herein, it is argued that the optimal use of abundant bioresources could well serve as a renewable feedstock for the chemical industry.[9] From a chemical perspective, renewable feedstocks, being highly functionalized molecules, are very different from fossil feedstocks which are generally unfunctionalized. Therefore, a huge challenge for chemists today is to provide the chemical industry with a new set of tools to convert renewables into useful chemicals in an economically viable fashion.[10,11] Here, we illustrate examples of two different approaches or strategies towards potential biomass-derived chemicals. It is proposed that the required cost-competitive and environmentally acceptable (sustainable) industrial chemical processes utilizing renewable starting materials are best achieved by the close integration of biocatalytic and heterogeneous catalytic processes.[12]

Fossil and Renewables Value Chains

Today, fossil resources are widely used to produce electricity, heat, and transportation fuels as well as the vast majority of the many chemicals that are required by contemporary society. During the 20th century, continuous scientific and technological developments led to ongoing refinements in these areas resulting in highly optimized and efficient technologies for utilizing fossil resources. Additionally, during the same period fossil resources were abundantly available at relatively low costs, and we can therefore talk of a fossil economy with re-

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spect to our society today. The aforementioned factors also mean that typically existing industrial processes are very cost-competitive when compared with emerging new technologies. Accordingly, significant efforts are required to develop such new alternatives into commercially viable solutions.[13]

Herein, we explore the prospects for using renewable resources, namely biomass, as an alternative to fossil resources as a feedstock for the chemical industry. In order to attempt to start identifying promising opportunities, it is instructive to establish a simple value chain that illustrates how the petrochemical industry transforms fossil resources into desirable products by a series of chemical transformations. The value chain in Figure 1 qualitatively illustrates the value of various

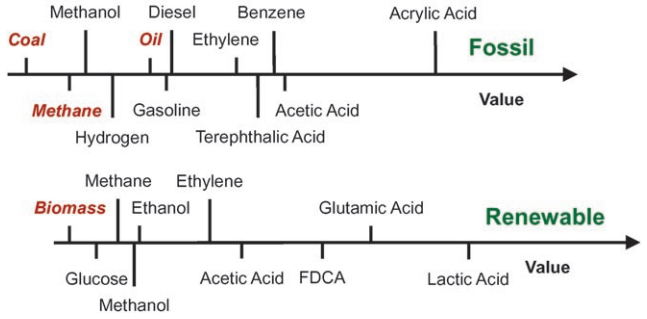

Figure 1. The fossil and renewables value chains indicate the value of different commodity chemicals relative to the feedstocks. A direct comparison between the two different value chains depends on the actual cost of the feedstocks.

important commodity chemicals relative to that of the fossil raw materials, that is, coal, natural gas, and crude oil.[14,15]

This is certainly a very simplistic illustration as the value of the fossil resources varies considerably, not only according to the geographic origin and quality but also over time for complex socio-economic reasons. Nonetheless, this fossil value chain for the chemical industry emphasizes that crude oil is transformed into transportation fuels by relatively simple, efficient, and inexpensive operations. Thus, transportation fuels are among the least expensive chemicals available.

In the petrochemical industry, fossil resources are used to produce important major chemicals; currently, the building blocks for about 95% of all the carbon-containing chemicals that are required to sustain our everyday lives. The majority of this wide range of specialized chemicals can be traced back to just seven basic building blocks. These building blocks—methanol, ethene, propene, butadiene, benzene, toluene, and xylene—can be considered as the backbone of the chemical industry.[16] The entire chemical industry is essentially constructed from these building blocks, a few of which are included in Figure 1. The fossil value chain illustrates that these building blocks are, typically, somewhat more valuable than transportation fuels and that the commodity chemicals produced from them can often be appreciably more so. The value of these bulk chemicals is essentially governed by the cost of the feedstocks and processing costs.

If we now envisage that the most important fuels and chemicals should instead be produced from biomass, then another value chain might materialize, as also depicted in Figure 1.[14] This value chain could be termed a renewables value chain for the chemical industry. As with the fossil resources chain, this is again only a qualitative evaluation for two main reasons: First, the cost and composition of the biomass feedstock will vary significantly from region to region; likewise, it will depend upon the source of biomass feedstock (e.g., food crops or waste products). In this respect, the situation differs not so greatly from that of fossil raw materials. Second, most of the chemical transformations required to establish a renewable chemicals industry are not yet developed to any major extent. In actuality, in many cases they still remain to be discovered. Thus, establishment of the renewables value chain is, to some extent, based on estimates. However, in some cases the relevant processes in this value chain can be identical to those in the fossil value chain.

In Figure 1, the fossil value chain and the renewables value chain are shown independently of one another, hence they cannot be directly compared. To directly compare the two value chains more quantitatively, it is necessary to know solely the cost of the compounds in the fossil and renewable feedstocks, assuming that the uncertainties related to the individual value chains are first handled properly as discussed. Figure 2

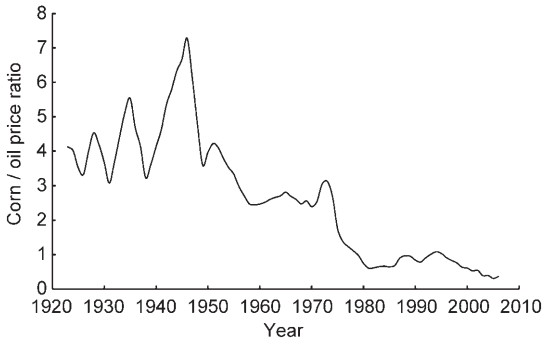

Figure 2. The plot of corn/oil price ratio during the last 80 years shows how biomass (corn) has become relatively cheaper and by that economically more interesting as an alternative to oil for the chemical industry.[14]

illustrates how the price of one specific fossil resource (crude oil) has varied relative to one specific renewable resource (corn) over time. Of special interest, during the last 80 years the corn/crude oil ratio has changed significantly but today it is at a historic low level. It is clear that if the cost of biomass feedstocks continues to decline relative to that of fossil resources, an increasing number of chemicals could be produced competitively from renewable resources.

However, it is important to be aware that the feedstock cost ratio will not change which products are the most attractive to produce from biomass; this depends exclusively on the relative values of the relevant compounds in the two different value chains. To develop an industry based on biomass is then simply a matter of developing the technologies that are best

able to compete with their fossil equivalents. Thus, from the value chains, it is possible to identify interesting first target chemicals that utilize the abundant biomass resources most efficiently, when establishing the foundation of a renewable chemicals industry. However, cost is not the only important parameter, as in many cases the potential to decrease CO_2 emissions on going from a fossil resource to a renewable resource will also hold significant importance. This is discussed briefly later, but here it is noted that this will vary significantly from one chemical on the two value chains to another. Accordingly, it would be fitting to also establish the exact amount of CO_2 produced, for instance, per kilogram of desired product (this could be termed a climate factor, or C factor, to remain consistent with the E factor introduced to indicate the overall amount of waste produced by chemical processes[17–18]). This C factor would help evaluate which renewable chemical processes are most desirable to develop under given boundary conditions.

From another perspective, the use of biomass as a sustainable resource for the production of fuels and chemicals should offer improved security in supply as biomass can be grown in most parts of the world. Conversely, oil resources are limited by being located only in a few, and in some cases, unstable areas of the world.[19] In conclusion, it appears very attractive to attempt to convert biomass into high value-added products rather than into relatively low-value fuels, in particular if this can be done in only a few and highly efficient process steps.

Prior to fossil resources becoming widely and inexpensively available, much of the chemical industry was based mostly on renewable raw materials. However, as these processes have not been continuously improved (as a result of unfavorable feedstock costs), they are generally not competitive with modern processes that rely on fossil resources. Nevertheless, in some case it has proven beneficial to explore biomass resources as raw materials and it could be even more attractive in the future.[20] This is typically the case in the production of key chemicals that have structures and functionalities which are very similar to those of the biomass feedstock.[21,22]

An economic evaluation of ethylene produced from steam-cracking of petroleum fractions and from the dehydration of bioethanol showed that the bio route was about 10–40% more expensive than the petroleum route to ethylene.[23] This study was carried out in 1988, with an oil price of about US$ 30/bbl (bbl = barrel; inflation adjusted) and a very well-established steam-cracking process. On the other hand, the production of bioethanol by fermentation of carbohydrates was not as developed as it is today. So, with today's oil prices around US$ 65–100/bbl and improved technology in the fermentation of biomass to ethanol, the route to bio-ethylene is becoming increasingly economically viable as compared to the route to petro-ethylene, and will continue to do so.

Today, all ethylene is still produced from fossil resources with the steam-cracking of naphtha as the main route. Ethylene has a price of more than US$ 1000/t[15] (metric ton = 1000 kg) and the price can only increase with the depletion of crude oil and increasing ethylene demands, in particular in China and India. Fuel-grade bioethanol has a price of less than US$ 600/t, clearly indicating that a relatively cheap dehydration process for ethanol to ethylene has good economic potential. Moreover, anhydrous ethanol is not necessary for the dehydration reaction,[23] thus the price for the bioethanol feedstock could be even lower as the expensive distillation to fuel-grade ethanol can be avoided.

A process that perhaps could be even more economically interesting is the oxidation of bioethanol to acetic acid. Acetic acid has today a value of around US$ 1400/t, which means that it is three times as expensive as fuel-grade ethanol on a molar basis. Again, it is not necessary to use anhydrous ethanol to produce acetic acid,[37] thus additionally favoring the bioprocess. These considerations lie behind the actual positions of ethylene and acetic acid in the renewables value chain (Figure 1) which we believe might be produced cheaper from renewable resources than from fossil resources.

Routes to a Renewable Chemicals Industry

In principle, it is possible to categorize the possible routes to establish a renewable chemicals industry into two distinctly different approaches, which should be pursued simultaneously. This categorization is presented in more detail here, and selected recent examples of both approaches are highlighted. It is shown how this categorization can be linked to the previously introduced value chains, and the barriers impeding the implementation of promising examples are discussed for the two different methods. In all likelihood, the future chemical industry will rely upon renewable chemicals fashioned from both approaches. In the first approach, biomass feedstocks are used to supply a proportion of the chemical building blocks that are currently produced from fossil resources, that is, the chemicals generically termed petrochemicals owing to their origin. The second approach is to target new chemicals, which have properties that make them potential substitutes for current petrochemicals.

Biomass Chemicals Identical to Current Petrochemicals

Figure 3 illustrates the current primary building blocks in the chemical industry derived from fossil resources (coal, natural gas and oil) and consequently used as building blocks for a range of significant large-scale commodity chemicals (shaded in dark gray). Syngas is produced from natural gas, along with ethylene and propylene, and is used to produce methanol on a large scale. In turn, methanol is used to produce commodity chemicals such as acetic acid and formaldehyde. Ethylene, along with other liquefied refinery gases such as propanes (propane and propylene), butanes (isobutylene and butadiene), and pentanes, is typically obtained by steam-cracking of naphtha, one of the largest industrial chemical processes today. As steam-cracking is endothermic and conducted at a very high temperature of around 750–875 °C, large amounts of fossil resources are required to heat the reaction mixture and to supply the heat of reaction. In fact, a mere 20% of the heat input to the steam-cracking process is used in the chemical conversion to olefin products; hence, there is a significant co-

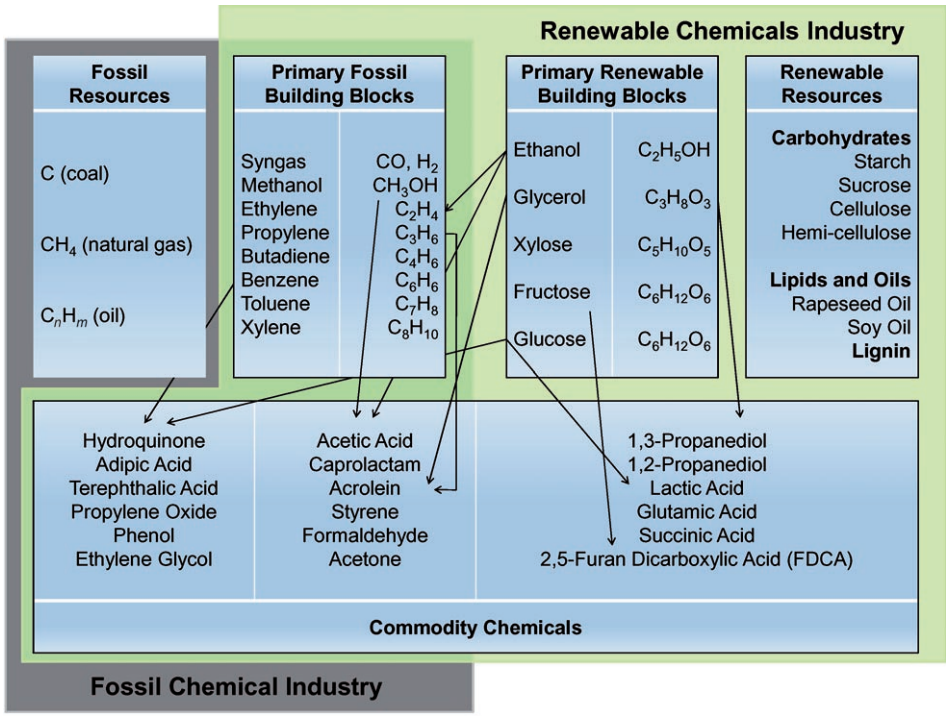

Figure 3. Strategies for producing commodity chemicals from biomass. The part set on a gray background shows some of the currently most important commodity chemicals produced from fossil resources. By strategy 1, these same chemicals are produced from renewable building blocks. Strategy 2 covers the idea of producing alternative chemicals, which potentially can substitute some of the "old" chemicals. Together strategies 1 and 2 cover the parts shown on the green background.

production of carbon dioxide. Accordingly, the C factor for the production of ethylene and propylene by steam-cracking is 0.65.[24] Ethylene is used to produce a wide range of chemicals, including ethylene glycol and styrene (with benzene via ethylbenzene), and it is also used directly as a monomer in polymers such as polyethylene and poly(ethylene terephthalate) (PET). Propylene is used to produce propylene glycol (1,2-propanediol), acrolein, acrylic acid, and acrylonitrile, and it is also used in the production of polymers. Benzene, toluene, and xylenes are derived from crude oil. Benzene is used to prepare commodity chemicals such as styrene, hydroquinone, phenol and acetone (both produced via cumene), and adipic acid and caprolactam (both produced via cyclohexane). The main outlet for xylene is in the production of terephthalic acid, which is used on a large scale for PET plastics.

Importantly, as is also illustrated in Figure 3, the primary building blocks described above can in principle also be produced from bioresources, and therefore, the commodity petrochemicals available today will also be available in the renewable chemicals industry. However, the production of these primary building blocks from bioresources will in some cases require more transformation steps as the natural primary renewable building blocks are newcomers to the commodity chemicals market. Nevertheless, biomass-derived syngas is an example of a primary fossil building block that is readily available from renewable resources by either gasification of biomass[25–27] or by aqueous-phase reforming of carbohydrate resources. However, instead of steam-reforming carbohydrates into syngas, they can also be transformed into simple sugars and fermented into building blocks such as ethanol and glycerol. Ethanol can be used to produce ethylene and butadiene (see below), and benzene, toluene, and xylenes can in turn be produced from ethylene by acid-catalyzed oligomerization.

Note that only selected chemicals are included in Figure 3, so as to focus on the synthesis strategy rather than on the exhaustive number of compounds that are produced in today's chemical industry or on the overwhelming number of possible routes to obtain these chemicals from bioresources. To outline the approach in more detail and to illustrate some recent examples of research efforts to develop new efficient routes to biomass-derived chemicals, a few selected synthesis pathways to major chemicals are highlighted with arrows. In the left part of Figure 3, the arrows connecting the fossil resources with various compounds illustrate how a given chemical is produced industrially today. On going from the top-right section of the diagram to the bottom left, the arrows indicate how it can be envisaged that the same compounds could instead be produced from renewable resources.

By way of an example, the acrylic acid family is explored in which acrolein is the key petrochemical intermediate. Acrylic acid is produced by the oxidation of propene in heterogeneously catalyzed processes, either directly or via acrolein in a two-step process. In terms of its usage, more than 90% of the acrylic acid is consumed as intermediates in the production of acrylate esters, which find widespread use as polymers, including superabsorbent polymers, detergents, adhesives, and coatings. Recently, the manufacture of acrolein from glycerol has received significant attention.[28] This is attributed to the fact that glycerol could become widely and inexpensively available as a by-product (or eventually even a waste product) from the production of biodiesel by transesterification. Indeed, it has been estimated that if the production of biodiesel grows as projected, the amount of glycerol available will rapidly be more than ten times higher than the current demand.[29] Alternatively, glycerol can be produced, for example, by the fermentation of glucose,[30] which could also develop into a cost-competitive process provided that the biodiesel market does not develop as quickly as projected. It is well known that by dehydrating glycerol, for example, with finely powdered $KHSO_4$ and K_2SO_4, it is possible to obtain acrolein in reasonable yields.[31] Through further developments, recently, several research

groups have reported that glycerol can be effectively dehydrated over solid acid catalysts to furnish acrolein in continuous processes with high yields,[32,33] and that acrolein can be oxidized to methyl acrylate in good yields even at ambient conditions.[34] Thus, the production of acrolein, and therefore also derivatives such as methyl acrylate, from glycerol obtained by fermentation will entail both biochemical as well as chemical process steps. In summary, acrolein could also be a key intermediate in the renewable chemicals industry.

Another example of integrated biochemical and chemical processes is the production of hydroquinone. Its production is currently mainly based on the oxidation of *para*-diisopropylbenzene (*p*-DIPB), which is available from Friedel–Crafts alkylation of benzene with propylene. *p*-DIPB is oxidized to the dihydroxyperoxide, which is cleaved to yield hydroquinone and acetone by an acid-catalyzed Hock rearrangement. Currently, the annual world production of hydroquinone is around 43 000 t. It has been reported that a benzene-free synthesis of hydroquinone is possible through biological pathways from glucose. The first approach proceeds by the shikimate pathway,[35] which requires 18 enzyme-catalyzed steps and one chemical step. However, a new approach to produce hydroquinone from glucose could be achieved in two enzyme-catalyzed steps and two chemical steps via 2-deoxy-*scyllo*-inosose synthase, thereby increasing the potential of the biosynthetic production of aromatic chemicals from glucose.[36]

A final example relates to the possibilities for using bioethanol as a feedstock for the chemical industry rather than, or as an alternative to, using it as a fuel additive. Ethanol can be thought of as a raw material for numerous industrially important chemicals, including ethylene, acetic acid, butadiene, and hydrogen.[14,37] As several of these transformations will be chemical processes, many of the chemicals produced from ethanol in the future will rely on integrated chemical and biochemical processes.

Originally, ethylene was manufactured primarily by the dehydration of ethanol[38] and similarly butadiene was produced from ethanol.[39,40] Today, acetic acid is still manufactured from ethanol. However, the major industrial process for the production of acetic acid is the carbonylation of methanol. Both methanol and carbon monoxide are typically produced by the steam-reforming of methane, which is a significantly endothermic reaction that takes place at temperatures above 600 °C. Approximately one quarter of the methane is directly combusted to heat the reactants and supply the heat of the reaction. Accordingly, about 0.6 kg CO_2 is produced for each kilogram of acetic acid, and the manufacture of acetic acid by this approach can therefore be said to have a C factor of about 0.6.

Alternatively, it can be conceived that acetic acid could be produced by the catalytic oxidation of ethanol. From the fossil and renewables value chains, it is observed that acetic acid is a relatively high-value commodity chemical, which is, say, twice as expensive as gasoline. In recent studies, acetic acid has been furnished in very high yields from the aerobic oxidation of ethanol in either liquid-phase[37] or gas-phase[41] processes using heterogeneous catalysts. In such new processes, it will be necessary to achieve optimal process integration so that energy-efficient handling of the large amount of water required in the fermentation is properly handled. With bioethanol available at lower prices than gasoline, a viable alternative technology for supplying acetic acid is available and could be cost-competitive and also lead to substantially lower CO_2 emissions than those reached when using bioethanol as a fuel additive.

In the manufacture of the chemicals described above, the chemical identity of the major building blocks remains unaltered when the feedstock is shifted from fossil to renewable, therefore resulting in only a modest impact on the rest of the chemical industry. As a result, the barriers presented for introducing such biomass-derived chemicals are expected to be relatively low. The focus in this approach will be on supplying the desired major chemicals at the lowest possible cost—and with the least possible environmental impact. This will require further development of efficient routes to transform biomass into useful starting materials, and here the technological developments driven by the demand for biofuels will be of appreciable importance. It appears that intimate integration of the involved biological and chemical processes is required to maximize energy efficiency, and thus this integration will be at least as important as it is in today's chemical industry.

Alternative Biomass Chemicals as Substitutes for Current Petrochemicals

The second approach towards realizing a renewable chemical industry is to produce chemicals from biomass that might potentially replace current petrochemicals. In its nature, this strategy is more visionary and will be harder to implement than the approach described above owing to the fact that such potentially new commodity chemicals are not already part of the existing markets. Therefore, cost will also become an important factor here in order for the new biomass-derived chemicals to compete with current petrochemicals and thus find an initial niche in the market. Likewise, environmental considerations need to be factored in—the new chemical should be manufacturable in a sustainable manner without the CO_2 emission problems currently encountered in the production of petrochemicals, otherwise the concept of introducing biomass as a sustainable replacement for fossil resources has little sense.

However, the concept of redesigning our chemical industry with replacement chemical commodities, designed in both process and final structure from today's know-how and technologies, is indeed an exciting one. The possibility to find biomass substitutes that are not only furnished from renewable feedstocks but involve a more efficient manufacturing process, and are maybe even more sustainable, stands as high. Examples of this approach include chemicals such as 2,5-furandicarboxylic acid (FDCA), lactic acid, and 1,2- and 1,3-propanediols, all of which are discussed here in some detail. In Figure 3, on going from the top right to the bottom right of the diagram, a pathway can be followed from renewable resources and primary building blocks to some of these potential replacement chemicals originating from biomass. Again, only a selection has been included for clarity.

Lactic acid and its polymer, poly(lactic acid) (PLA), are taken as first examples to further illustrate this approach as it is an example of a biomass chemical that has already entered the market as an alternative to fossil-derived polymers such as PET and polystyrene. The monomer, lactic acid, is produced by bacterial fermentation from cornstarch or sugar, and PLA is mostly manufactured by polymerization of its cyclic dimer lactide. The current production capacity for PLA is 450 000 tons per annum, however, this is projected to increase significantly in the coming years. PLA polymers are now used as biodegradable alternatives for packaging purposes and as fiber materials and could very well become economically competitive alternatives on a larger scale in the future. The major advantage of PLA polymers is the fact that they are fully biodegradable and compostable, and the degradation products, lactic acid and CO_2, are of course easily assimilated into biological systems. In fact, owing to the ease of absorbability, PLA polymers have been used for decades in the medical industry as, for example, resorbable implants and sutures.

FDCA is another example of a biomass chemical that could find use as a replacement monomer for making PET-type plastics. It can be produced from carbohydrates such as glucose and fructose that can undergo dehydration in the presence of acidic catalysts to form 5-hydroxymethylfurfural (HMF),[42,43] which under mild conditions can be oxidized to FDCA. This has been achieved using various strategies: notably, it has been shown that a silica-supported cobalt catalyst performs the dual task of dehydration to form HMF in situ and aerobic oxidation of HMF to furnish FDCA directly from fructose.[44] An alumina-supported platinum catalyst[45,46] as well as a titania-supported gold catalyst[47] have also been reported as effective catalysts for the oxidation reaction, although in the latter case the dimethyl ester is produced instead of the dicarboxylic acid. However, there are several obstacles to overcome for FDCA to become a viable alternative monomer in the production of PET-type plastics, namely that it remains to be demonstrated that polymers with the desired properties can indeed be made from FDCA on a large scale. Another limiting factor to the use of FDCA is the current high cost of dehydrating carbohydrates and purifying HMF.

Both isomers of propanediol are also examples of biomass chemicals that are expected to find increasing application in the future. They can both be produced from glycerol, which, as discussed above, might become an increasingly important renewable chemical in the future.[30] Although 1,2-propanediol is a petrochemical, which is typically produced in quantities exceeding 500 000 tons per annum by hydration of propylene oxide, its use for several applications is impeded by its current cost relative to ethylene glycol. However, as 1,2-propanediol can be produced in high yield by hydrogenation of glycerol,[48] it could become competitive to ethylene glycol in the future for selected applications, for example, as an antifreeze agent. Contrarily, 1,3-propanediol is not readily available from petrochemical feedstocks. However, in recent years, fermentation routes to 1,3-propanediol have been developed either from glycerol[49] or from glucose,[50] making this biomass chemical available at competitive cost. It has now found application as one of the monomers of poly(trimethylene terephthalate), a high-performance polyester material, under trade names such as Sorona 3GT (DuPont) and Corterra (Shell).

In the future, more examples of this approach will appear. Even though it can be more difficult with this approach to penetrate markets, it might be the strategy that ultimately leads to the most sustainable use of our limited bioresources.

Conclusions

Establishment of a renewable chemicals industry in which biomass is transformed into high-value-added chemicals might be the most advantageous way to secure optimal use of our abundant, but limited, bioresources from both an economical and ecological perspective. To evaluate the economical potential of new processes that transform biomass into desirable chemicals, we propose that the fossil and renewables value chains can be useful tools. Another important factor to consider in targeting the production of chemicals from renewable resources is the reduction in CO_2 emissions that might be achieved by the new technology. We put forward that the use of C factors could be a simple, convenient, and instructive method to facilitate such comparisons. Finally, it is noted that the establishment of a renewable chemicals industry appears to require an intimate integration of biocatalytic and heterogeneous catalytic processes to ensure that profuse bioresources are transformed into useful chemicals in a cost-competitive way, coupled with having minimum impact on the environment. Undoubtedly, the transition from a fossil chemical industry to a renewable chemicals industry will occur in many small steps. The rate at which these steps are taken evidently depends on the relative costs of renewable and fossil feedstocks, but also on requirements for introducing CO_2-reducing technologies. However, progress will likewise depend on our ability to focus research and development efforts on the most promising alternatives. In this aim, we hope that the present discussion might contribute to identifying suitable first targets in a more lucid manner.

Acknowledgements

The Center for Sustainable and Green Chemistry is sponsored by the Danish National Research Foundation.

Keywords: industrial chemistry · renewable resources · sustainable chemistry

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Received: December 21, 2007
Published online on March 25, 2008

Heterogeneous catalysis for production of value-added chemicals from biomass

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DOI: 10.1039/b712664f

1. Introduction

Almost everything around us is in some way a product of controlled chemical processes. That is either chemical processes conducted in Nature or chemical processes conducted in the chemical industry. In the most developed parts of the World, it is in fact products from the chemical industry that completely dominate our everyday lives. These products range from fuels and fertilizers to plastics and pharmaceuticals.[1] To make these products widely available, a huge amount of resources have been invested during the last century to develop the chemical industry to its current level where it is the largest industry worldwide, a cornerstone of contemporary society, and also a platform for further global economic growth.[2,3] It can be argued that the enormous success of the chemical industry can be attributed to the almost unlimited availability of inexpensive fossil resources, and to a continuously increasing number of catalysts and catalytic processes that make it possible to efficiently transform the fossil resources into all the required compounds and materials. Accordingly, more than 95% of the fuels and chemicals produced worldwide are derived from fossil resources, and more than 60% of the processes and 90% of the products in chemical industry somehow rely on catalysis. It has been estimated that 20–30% of the production in the industrialized world is directly dependent on catalytic technology.[4] Therefore, it is not surprising that we are continuously expanding our already vast empirical knowledge about catalysis to further improve the efficiency of existing catalysts and processes, to discover entirely new ways of valorizing available resources, and to lower the environmental impact of human activities.[5] Due to the overwhelming importance of fossil resources during the 20th century, most catalysis research efforts have, so far, concerned the conversion of these resources into value-added fuels and chemicals. There are, however, indications that the era of easy access to inexpensive fossil resources, especially crude oil, is coming to an end. The resources are certainly limited and the demand from everywhere in the world is growing rapidly. At the same time, it is becoming increasingly clear that the emission of CO_2 that follows the use of fossil resources is threatening the climate of the Earth. Together this makes the development of a chemical industry based on renewable resources one of the most important challenges of the 21th century.

This challenge has two different facets. One is the discovery and development of methods to use renewable resources to supply suitable energy carriers, in sufficient quantities at acceptable costs, and with minimal impact on the environment. The other is the discovery and development of new ways to provide all the chemicals needed to sustain a modern society. Whereas there are several possible energy scenarios that do not involve carbon-containing energy currencies, it is in fact impossible to envisage how it should be possible to provide the required chemicals and materials without relying extensively on carbon-containing compounds. Thus, to develop a chemical industry that does not depend on fossil resources, there are only two alternative carbon sources and that is CO_2 and biomass. Since transformation of CO_2 into useful chemicals always requires a significant energy input and since

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it is usually only available in minute concentrations, it appears attractive to instead utilize biomass as the dominant feedstock for chemical industry. In this way, it is possible to harvest the energy input from the Sun that is stored by photosynthesis in the C–C, C–H, C–O, and O–H bonds of the biomass. Clearly, a shift from fossil resources to renewable resources as the preferred feedstock in chemical industry is a formidable challenge. However, it is worth pointing out that during the early part of the 20th century, before fossil resources became widely available, biomass was the preferred feedstock for the emerging chemical industry, and today, biomass still finds use as a feedstock for a range of very important chemicals.[6] Interestingly, these processes often rely mostly on the availability of biological catalysts whereas the processes for conversion of hydrocarbons use mostly heterogeneous catalysts. However, to explore the full potential of biomass as a feedstock in chemical industry, it appears necessary to integrate processes that rely on biological catalysts with processes that use heterogeneous or homogeneous catalysts to develop new, cost-competitive and environmentally friendly technologies.[7] Here, we will survey the possibilities for producing value-added chemicals from biomass using heterogeneous catalytic processes.

2. Setting a new scene

2.1 Biomass for production of fuels and chemicals

Currently, there exists a strong focus on the manufacture of transportation fuels from biomass.[8,9] Clearly, this can be attributed to a desire to relinquish our dependence on fossil fuels, in particular crude oil, and also to significantly lower the emission of greenhouse gasses to minimize global warming. In some regions of the world, it seems that production of bio-ethanol is indeed already cost-competitive with gasoline[8] and this demonstrates the potential of biomass as a renewable raw material. However, it is also clear that widespread use of biomass as a raw material for biofuel production remains controversial from both an economical and an ecological perspective. These issues must, of course, be resolved soon in a fully transparent way to identify sustainable paths forward. However, it is undisputable that we will eventually need alternatives to the fossil resources for producing chemicals and materials.[9–11] It can be argued that if the amount of biomass available is too limited to substitute fossil resources in all its applications and if sufficiently efficient methods for transforming biomass into value-added chemical can be developed, this will represent the optimal use of biomass.[7] There are two reasons for this. First of all, most chemicals, even most of the simple petrochemical building blocks, are significantly more valuable than transportation fuels. This can be illustrated in a semi-quantitative way by comparing the value chains in a chemical industry based on fossil and renewable resources, respectively.[7] In this context, it is instructive to compare the cost of renewable resources to fossil resources over time. It is noteworthy that today, the cost of glucose is comparable to the cost of crude oil (on a mass-to-mass basis). Secondly, it is clear that by use of renewable resources as a feedstock for the chemical industry, significantly higher reductions in the emissions of green-house gases can be achieved than what is possible by production of biofuels. This can be attributed to the fact that production of many large-scale commodity chemicals from fossil resources is associated with a substantial co-production of CO_2 as expressed *e.g.*, by the C-factor (kg CO_2 produced by kg of desirable product).[7] This can often be attributed to the high temperature required to transform hydrocarbons. To illustrate this, the C-factor for industrial production of hydrogen from natural gas is about 9 and for ethylene from naptha it is 0.65. If hydrogen or ethylene was produced efficiently from biomass, the C-factor would approximately express the amount of CO_2 emission that would be saved compared to what would be possible by production of biofuels instead. Since ethylene alone is currently

produced in an annual amount close to 100 mill. ton, it is obvious that this would have a substantial impact on the total emission of green-house gases.

2.2 Biomass in chemical industry

There are many ways in which biomass can be envisaged to become an increasingly important feedstock for the chemical industry, and this has already been the topic of numerous studies.[10–22] The most comprehensive study was published recently by Corma *et al.*[10] and it contains a very detailed review of possible routes to produce chemicals from biomass.

In Fig. 1, we illustrate schematically how selected commodity chemicals could be produced using abundant bio-resources, *i.e.*, carbohydrates (starch, cellulose, hemicellulose, sucrose), lipids and oils (rapeseed oil, soy oil, *etc.*), and lignin as the sole raw materials. From these bio-resources, it is possible to directly obtain all the compounds classified in Fig. 1 as primary renewable building blocks (of which only selected examples are given) with only one purification step. For example, ethanol can be obtained by fermentation of sucrose, glucose by hydrolysis of starch, glycerol by transesterification of triglycerides (or by fermentation of glucose), xylose by hydrolysis of hemi-cellulose, fructose by hydrolysis of sucrose (and by isomerization of glucose), and finally synthesis gas can be obtained directly by gasification of most bio-resources or by steam-reforming of the other primary renewable building blocks. From the primary renewable building blocks a wide range of possible commodity chemicals can be produced in a single step, and again examples of selected transformations are shown in Fig. 1. For instance, acetic acid can be produced by fermentation of glucose or by selective oxidation of ethanol. Lactic acid is available by fermentation of glucose, and 5-hydroxymethyl furfural can be obtained by dehydration of fructose. These compounds can again be starting materials for other desirable products and so forth. Some of the commodity chemicals shown are already produced on a large scale from fossil resources, *e.g.*, ethylene, acetic acid, acrolein and butadiene. Others are envisaged to become important large-scale commodity chemicals in the future when biomass gradually becomes a more

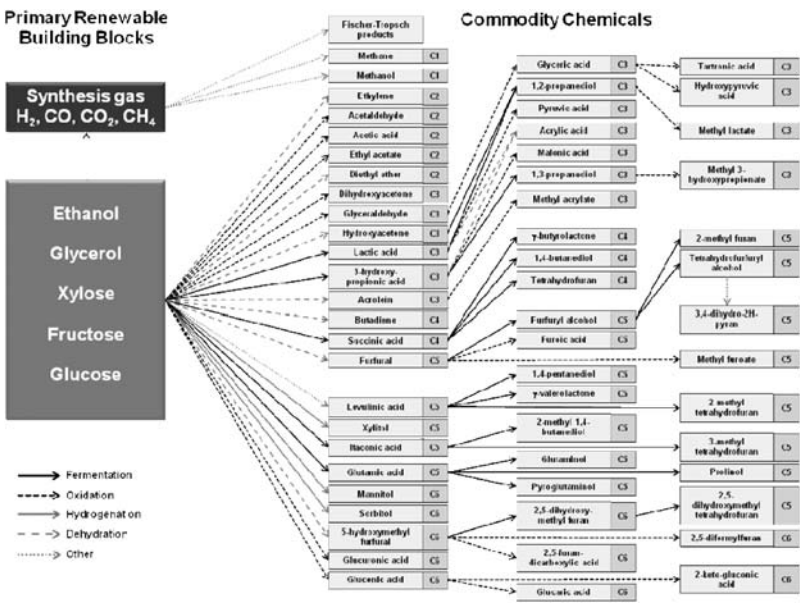


Fig. 1 Overview of how selected commodity chemicals could be produced from primary renewable building blocks.

important feedstock.[14] The different commodity chemicals are labeled using different colors to categorize them according to their number of carbon atoms. It is seen that a wide range of C_1 to C_6 compounds can be made available by quite simple means. Moreover, the chemical transformations in Fig. 1 are labeled with colored arrows to illustrate specific ways to convert one building block into another. As it is apparent, the reactions all require a suitable catalyst, and this can be either a biological catalyst or a heterogeneous/homogeneous catalyst. Most of the primary renewable building blocks are produced today from bio-resources using mainly biocatalytic processes, and similarly several of the proposed commodity chemicals can also be produced from the primary renewable building blocks using biological catalysts. On the other hand, it is also clear that a very substantial number of the desirable transformations rely on the availability of suitable heterogeneous or homogeneous catalysts. Thus, it appears likely that a chemical industry based on renewable resources as the dominant feedstock will feature biological and chemical processes intimately integrated to efficiently produce all the desired chemicals and materials.

2.3 Heterogeneous catalysis and biomass

Often, it appears that the possible role of heterogeneous catalysis in this scenario is not receiving sufficient attention in comparison with that of the biocatalytic methods. Therefore, in the present chapter we will highlight some of the existing possibilities for converting bio-resources, primary renewable building blocks, and commodity chemicals derived from these into value-added chemicals. We will focus on production of chemicals that can prove useful on a larger scale since they will contribute most to the valorization of significant quantities of biomass, and thereby contribute most to relinquishing the dependence on fossil fuels and to lowering the emission of green-house gases. Hopefully, this will be useful as a starting point for others to discover and develop new reactions and catalysts that can become useful in the efforts to make biomass a more useful resource for chemical industry. Our emphasis here is the catalytic reactions and the corresponding catalysts. Therefore, we have organized the literature covered in separate chapters according to five important reaction types, specifically, C–C bond breaking, hydrolysis, dehydration, oxidation, and hydrogenation. We envisage that these reaction types will be the most important for producing value-added chemicals from biomass since they can be conducted on large scale and they do not involve expensive reagents that will make them prohibitively expensive for industrial applications. Clearly, other reactions will also be important but several of those will be analogues to current methods in chemical industry. In each chapter, the presentation is organized hierarchically to first discuss the catalytic conversion of compounds that are most closely related to the bio-resources (carbohydrates, lipids and oils, and lignin) and then successively those derived from these renewable raw materials.

3. Catalytic C–C bond breaking

3.1 Introduction

This section concerns catalytic processes that transform chemicals from renewables by C–C bond breaking. Among these are thermochemical processes, such as pyrolysis and also gasification, catalytic reactions, such as catalytic cracking and different reforming reactions, and decarbonylation and decarboxylation reactions. Many of these reactions occur simultaneously, particularly in the thermochemical processes. Another technically important class of C–C bond breaking reactions is the fermentation processes, however, they will not be considered in this section since they do not involve heterogeneous catalysis.

3.2 C–C Bond breaking reactions involving bio-resources

3.2.1 Crude biomass. Next to combustion, gasification is probably the easiest and most primitive method for degradation of biomass. In the simplest form, gasification involves heating of biomass (or any other carbonaceous material) to temperatures around 800–900 °C, in an atmosphere with only little oxygen, until it thermally decomposes into smaller fragments. This partial oxidation process obviously requires a significant energy input and is not particularly selective; on the other hand, it is reasonably flexible since essentially all types of biomass can be gasified. Gasification, in particular of coal, has been known for long and was previously used to produce town gas. However, the gas resulting from gasification has a relatively low heating value of only 10–50% of that of natural gas,[23–25] and this was a major reason for replacing town gas with natural gas. During World War II, biomass gasification advanced in Europe, but it was not until the oil crisis in the 1970s that new developments in the area truly took place.[24] Today, the main purpose of biomass gasification is to produce synthesis gas, with a $H_2:CO$ ratio close to two, which is suitable for methanol synthesis or Fischer-Tropsch fuels.

There exist many different types of gasification furnaces but they generally work by having several different cracking and reforming zones. These zones are typically a pyrolysis zone, an oxidation zone and a reduction zone. Biomass is broken down either by pyrolysis (without oxygen) or by partial oxidation (with oxygen or air as oxidant) to a mixture of CO, CO_2, H_2O, H_2, CH_4, other light hydrocarbons, some tar, char and ash, as well as some nitrogen and sulfur containing gasses such as HCN, NH_3, HCl, H_2S *etc*.[25] The hydrocarbons and the char are further partially oxidized to mainly CO and H_2O (1–4) and steam reformed (5–6) or dry reformed (7–9) to CO and H_2. The heat from the exothermic oxidation reactions is used to supply the heat for the endothermic cracking reactions. Finally, the $H_2:CO$ ratio can be adjusted by the water gas shift reaction (10).[23–26]

$$CH_4 + \tfrac{1}{2}O_2 = CO + 2H_2 \quad (1)$$

$$H_2 + \tfrac{1}{2}O_2 = H_2O \quad (2)$$

$$C_nH_m + (n/2 + m/4)O_2 = nCO + (m/2)H_2O \quad (3)$$

$$C + \tfrac{1}{2}O_2 = CO \quad (4)$$

$$C_nH_m + nH_2O = nCO + (n + m/2)H_2 \quad (5)$$

$$C + H_2O = CO + H_2 \quad (6)$$

$$C_nH_m + nCO_2 = 2nCO + (m/2)H_2 \quad (7)$$

$$C + CO_2 = 2CO \quad (8)$$

$$CH_4 + CO_2 = 2CO + 2H_2 \quad (9)$$

$$CO + H_2O = CO_2 + H_2 \quad (10)$$

The major challenge in gasification is to avoid the formation of tars, which have a tendency to clog filters and condense in end-pipelines. Tars are considered as the condensable fraction of the organic gasification products, and consist mainly of different aromatic hydrocarbons with benzene as the main species. For removal of tars three types of catalysts have been widely investigated; alkali metal salts, alkaline earth metal oxides and supported metallic oxides.[24–26]

Alkali metal salts can be mixed directly with the biomass before entering the gasification furnace. They enhance the gasification reactions and lower the tar content, but recovery of the catalyst is difficult and costly making the alkali metals unattractive as catalysts for industrial use.[25,26] Another family of catalysts, which can be used effectively for gasification, is the alkaline earth metal oxides and carbonates. Of these, mainly the naturally occurring mineral dolomite

($MgCO_3 \cdot CaCO_3$) has been used.[25] It enhances the degradation of especially the tars and hydrocarbons into light gasses, though it is not active for methane reforming. When dolomite is calcined at 800 °C, CO_2 is eliminated, yielding a far more active catalyst. These catalysts are deactivated by carbon formation and attrition but they are inexpensive and disposable, and therefore easily replaceable. The third type of catalysts used are metals on a support, typically nickel on various oxide supports. Nickel catalysts are highly effective in tar destruction, the reforming of hydrocarbons and in adjusting the composition of the synthesis gas by the water gas shift reaction (10). They are operated as secondary catalysts in a downstream reactor, which can be operated at conditions different from those in the gasifier. Nickel catalysts primarily deactivate due to carbon formation and nickel particle sintering. Therefore, dolomite is often used in guard beds upstream of the nickel catalyst bed to remove most of the higher hydrocarbons.[24–26]

Instead of gasifying biomass, it can be subjected to liquefaction in a pyrolysis process. Pyrolysis is actually one of the main processes occurring during gasification, however, in a dedicated pyrolysis plant, the desired products are liquid hydrocarbons rather than synthesis gas. In the current development of pyrolysis reactors, this is achieved by a fast pyrolysis process. Here, the biomass is heated rapidly to temperatures of around 500–600 °C, which leads to formation of a dark brown liquid known as bio-oil along with some gasses and chars. Other types of liquefaction processes are high pressure pyrolysis (350 °C, 20 MPa) and non-pyrolytic liquefaction (aqueous/non-aqueous) (250–425 °C, 10–35 MPa).[27] The liquid products from these processes are of relatively pure quality with a heating value of around half that of conventional oil. Alternatively to being used as heating oil they can be upgraded to transportation fuels or chemical feedstocks by hydrotreatment and catalytic cracking.

A possibly more sophisticated method for utilizing biomass to produce synthesis gas is by aqueous phase reforming (APR), a processing method that was developed for carbohydrates and other more readily accessible biomass oxygenates by Dumesic *et al.*[28–32] Valenzuela *et al.*,[33] however, were the first to report APR of real woody biomass. They used sawdust from pine, which was milled to an average diameter of 375 μm. The biomass was mixed with water, sulfuric acid (5%) and a catalyst (Pt/Al_2O_3) in a batch reactor. The acid catalyzed the hydrolysis of the biomass to decompose it into smaller soluble molecules, which were reformed over the platinum catalyst to yield mostly hydrogen and carbon dioxide. The process was operated at 225 °C, with hydrogen accounting for 33% of the non-condensable product gasses.

3.2.2 Bio-oils. In the 1970s, it was shown that bio-oils from plant extracts such as rubber latex, corn oil, and peanut oil can be converted into a mixture of mainly gasoline and liquid petroleum gas over a ZSM-5 catalyst, at temperatures between 400–500 °C.[34] These bio-oils were investigated as feedstocks for the reaction because they have high hydrogen to carbon ratios and low oxygen contents and therefore a hydrocarbon-like structure. It was suggested that such renewable plant resources, due to their siginifant content of highly reduced photosynthetic products, would be suitable for producing fuels or chemical raw materials.[35] The high hydrogen-to-carbon ratios in the biomass feed is desirable because oxygen usually must be removed and/or hydrogen must be added to achieve useful products.

Recently, several groups have investigated the catalytic conversion of bio-oils or model bio-oils over HZSM-5 catalysts,[36–38] and recently a review was published describing how biomass could be converted into fuels or chemicals in a conventional petrochemical refinery in FCC or hydrotreating refinery units.[39]

3.2.3 Carbohydrate resources. Carbohydrate resources, such as hydrolyzed starch and sucrose as well as xylose and glucose, can be processed into hydrocarbons in a process similar to the one performed with bio-oils as described above

(section 3.2.2), *i.e.* by using a HZSM-5 catalyst operated at around 510 °C and ambient pressure.[40] This process is perhaps a little surprising since carbohydrates do not resemble the desired hydrocarbon product as much as the bio-oils do. However, formation of hydrocarbon compounds was found to occur as a result of oxygen removal from the carbohydrate by decarbonylation and decarboxylation reactions.[40] This process is probably one of the first attempts to conduct catalytic cracking of biomass.

Carbohydrate resources have also been processed under hydrotreating conditions, *i.e.* high hydrogen pressures (35–300 bar) and high temperatures (300–600 °C) in the presence of Co–Mo or Ni–Mo-based catalysts; although other precious metals like Ru and Pt can also be used.[39] The main reaction involved under these conditions is hydrodeoxygenation (HDO), as, for example, described by Elliot *et al.*[41] The important advantage of this technology is that excellent fuels and useful chemicals can be produced in good yields, but the process is expensive and requires high hydrogen pressures.

3.3 C–C Bond breaking reactions involving primary renewable building blocks

3.3.1 Aqueous-phase reforming (APR). Aqueous phase reforming of glucose, glycerol and other biomass oxygenates, such as methanol, ethylene glycol and sorbitol, was carefully investigated by the group of Dumesic.[28–32] They showed how various biomass oxygenates can be converted into H_2, CO_2 and some light alkanes with good conversions and high selectivities over a Pt/Al_2O_3 catalyst operated at 225–265 °C and 29–56 bar,[28] as well as over a specially designed non-precious metal catalysts (Raney Ni–Sn).[29] It was shown that this reaction could be used to supply hydrogen that could simultaneously be used for reduction of sorbitol to hexane.[30] This was achieved using a bifunctional catalyst that caused sorbitol to be partly cleaved over a metal catalyst (Pt, Pd) to form H_2 and CO_2 and at the same time sorbitol was also dehydrated over a solid acid catalyst. By carefully balancing these reaction steps, the hydrogen produced could be used directly for hydrogenation of the dehydrated sorbitol to eventually yield alkanes.[30] Alternatively, hydrogen could be co-fed, whereby the production of CO_2 was avoided and the conversion to alkanes (especially hexane) is improved.[30]

3.3.2 Steam reforming of ethanol. Steam reforming (SR) is probably the most investigated process for breaking C–C bonds in chemicals available from biomass. Particularly, ethanol SR for production of hydrogen has been extensively examined,[42–44] but also other primary renewable building blocks have received attention, such as SR of glycerol[45,46] or SR of bio-oils.[47,48]

SR of methane/natural gas is one of the largest catalytic processes in the world and is by far the most important method for producing industrial hydrogen today. The process is well described in literature and it is typically carried out at 800–950 °C over nickel-based catalysts.[49] The main reactions are methane SR (11) and water-gas-shift (WGS) (12).

$$CH_4 + H_2O = CO + 3H_2 \quad (11)$$

$$CO + H_2O = CO_2 + H_2 \quad (12)$$

SR of ethanol has mainly been conducted under similar conditions as methane SR, which means relatively high temperatures, ambient pressure, and primarily with Ni- or Rh-based catalysts.[42–44] Ideally, one mole of ethanol is converted into 6 moles of hydrogen (13). During SR, ethanol decomposes mainly through two different routes; either by dehydrogenation to acetaldehyde (14) or dehydration to ethylene (15). These two intermediates can be further catalytically reformed to a thermodynamically equilibrated reaction mixture of H_2, CO, CO_2, CH_4 and H_2O (12, 16–18).[50]

$$CH_3CH_2OH + 3H_2O = 2CO_2 + 6H_2 \quad (13)$$

$$CH_3CH_2OH = CH_3CHO + H_2 \quad (14)$$

$$CH_3CH_2OH = CH_2CH_2 + H_2O \quad (15)$$

$$CH_3CHO = CH_4 + CO \quad (16)$$

$$CH_3CHO + H_2O = 3H_2 + 2CO \quad (17)$$

$$CH_2CH_2 + 2H_2O = 4H_2 + 2CO \quad (18)$$

A substantial difficulty in ethanol SR is a too rapid catalyst deactivation due to coking. This can occur by several reactions, such as methane decomposition (19) or the Boudouard reaction (20), but primarily the polymerization of ethylene is thought to cause the problems (21). Unlike the situation for methane SR, it appears that for ethanol SR the deactivation by coke formation is lower at high temperatures.

$$CH_4 = 2H_2 + C \quad (19)$$

$$2CO = CO_2 + C \quad (20)$$

$$CH_2CH_2 = \text{polymeric deposits (coke)} \quad (21)$$

SR of ethanol is an endothermic reaction and relatively high temperatures are required to convert ethanol into hydrogen and carbon monoxide and eventually carbon dioxide after equilibration by the WGS reaction (12). Thus, the drawback of this process is the energy requirements, which perhaps are not so disadvantageous. If the hydrogen is used in a high efficiency fuel cell, compared to combusting the ethanol in a motor engine with a relatively low efficiency, the overall energy output could be significantly improved.[50] Alternatively, the steam reforming reaction can be performed as a partial oxidation (22).[51] Less hydrogen is formed in this way, but instead the reaction is slightly exothermic, thus making hydrogen from renewable resources without the need of adding extra energy in terms of heat.

$$CH_3CH_2OH + 2H_2O + \tfrac{1}{2}O_2 = 2CO_2 + 5H_2 \quad (22)$$

3.3.3 Decarbonylation. Furfural is easily obtained from biomass waste such as oat and rice hulls that are rich in pentosans. Further valorisation of furfural can be done by decarbonylation to produce furan, which can be further converted into tetrahydrofuran by catalytic hydrogenation.

Pure decarbonylation typically employs noble metal catalysts. Carbon supported palladium, in particular, is highly effective for furan and CO formation.[52] Typically, alkali carbonates are added as promoters for the palladium catalyst.[52,53] The decarbonylation reaction can be carried out at reflux conditions in pure furfural (165 °C), which achieves continuous removal of CO and furan from the reactor. However, a continuous flow system at 159–162 °C gave the highest activity of 36 kg furan per gram of palladium with potassium carbonate added as promoter.[54] In oxidative decarbonylation, gaseous furfural and steam is passed over a catalyst at high temperatures (300–400 °C). Typical catalysts are zinc-iron chromite or zinc–manganese chromite catalyst and furfural can be obtained in yields of around 90% at full conversion.[53] Again, addition of alkali metal carbonates promotes the reaction.

3.3.4 Deformylation. Levulinic acid is used as a starting material for the preparation of organic chemicals, dyes, polymers, pharmaceutically active compounds and flavoring agents. Acidic catalysts are required to procure levulinic acid from sugars, and/or 5-HMF. Acidic ion-exchange resins have been tested for

dehydration of sucrose in pure water at 100 °C.[55] And levulinic acid could be achieved with up to 83% selectivity using all four tested ion-exchange resins (Dowex MSC-1H, Amberlyst 15, Amberlyst XN-1010 and Amberlyst XN-1005) although the overall yields were quite low (9–24%) even after 24 h reaction times.[55] Better results were achieved using zeolites as catalysts. Zeolite LZY was tested for fructose dehydration in pure water at various temperatures with the main product being levulinic acid formed in *ca*. 66% yield after 15 h at 140 °C.[56] Levulinic acid was also observed as one of the main products from aqueous phase dehydration of glucose using zeolite H-Y (with a SiO_2/Al_2O_3 ratio of 6.5) as well as with acidic montmorillonite clays as catalysts,[57,58] but significantly lower yields were reported. With the possibilities of levulinic acid as a renewable chemical building block, it seems interesting to develop the zeolite-catalyzed process from cellulosic feedstocks.

3.3.5 Hydrogenolysis. C–C and C–O bond breaking by hydrogenolysis of different polyols (glycerol, xylitol, erythritol and sorbitol) has been investigated by Montassier *et al*.[59,60] Predominantly ruthenium and copper-based charcoal catalysts were studied at 210–260 °C and 1–6 MPa hydrogen pressures. The main products from the aqueous glycerol conversions were propylene glycol using copper catalysts and ethylene glycol along with methane using ruthenium catalysts. The hydrogenolysis of glycerol to ethylene glycol and propylene glycol using ruthenium on a range of different supports at 180 °C and 5 MPa hydrogen pressure showed the highest conversion on a TiO_2 support.[61] Blanc *et al*. reported the treatment of aqueous sorbitol solutions on CuO–ZnO catalysts at 180 °C 130 bar hydrogen pressure.[62] The purpose of the analysis was to achieve a high C_{4+} selectivity suitable in the synthesis of alkyd polymers, and the CuO–ZnO catalyst was superior in achieving a high C_{4+} selectivity (73% yield) compared to Ru and Ni catalysts which mainly yielded C_1–C_3 products.

A commercial example of a hydrotreating technology is examined below. The IPCI (International Polyol Chemicals, Inc.) hydrogenolysis process is carried out at 100–300 °C and at hydrogen pressures of 70–300 bar.[63] The hydrogenolysis process is used to cleave carbohydrates to smaller polyol fragments. Specifically, sorbitol and mannitol are reformed to propylene glycol and ethylene glycol as the main products, and to different butanediols in smaller quantities.[64] The primary product, propylene glycol, is formed by hydrocracking either of sorbitol directly (23) or, more likely, through glycerol (24,25).

$$C_6H_{14}O_6 + 3H_2 = 2C_3H_8O_2 + 2H_2O \quad (23)$$

$$C_6H_{14}O_6 + H_2 = 2C_3H_8O_3 \quad (24)$$

$$C_3H_8O_3 + H_2 = C_3H_8O_2 + H_2O \quad (25)$$

The composition of the hydrogenolysis products is very dependent on the actual process conditions and on the catalysts used in the reaction. So far, mostly supported nickel catalysts are being applied. IPCI has constructed a 10 000 MT/y pilot plant in China in 2005, and in 2007, a commercial 200 000 MT/y plant was commissioned, also in China.[63]

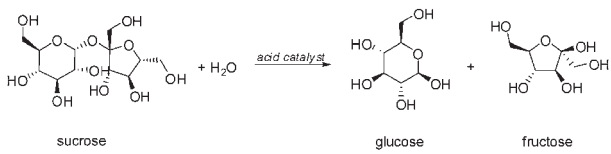
4. Catalytic hydrolysis

4.1 Introduction

Hydrolysis is the process by which a compound is broken down by reaction with water, thus it can be thought of as the opposite reaction of dehydration, where water is of course removed. Hydrolysis is a key reaction type in biomass chemistry, for it is central in the depolymerisation of polysaccharides to simpler monosaccharide building blocks, such as fructose, glucose, and xylose.

4.2 Hydrolysis reactions involving renewable resources

4.2.1 Sucrose, maltose and cellubiose. Sucrose can be hydrolyzed to give inverted sugars, *i.e.* a mixture of fructose and glucose (Scheme 1). For the transformation of biomass into value-added chemicals, this is a key reaction since it provides major building blocks for further chemical synthesis, fructose and glucose, from widely occurring sucrose. In the past, and on an industrial level, this reaction has been performed with the use of enzymes as the catalyst. However, due to the production of waste, low thermal stability, problems with separation of products and enzymes, and recovery, and low rate due to glucose and fructose inhibiting the reaction, a different path has been sought for.



Scheme 1 Sucrose is hydrolyzed into a mixture of glucose and fructose when exposed to an acid catalyst. Sulfuric acid has been used for this, but also heterogeneous solid acid catalysts have found use, especially acidic ion exchange resins.

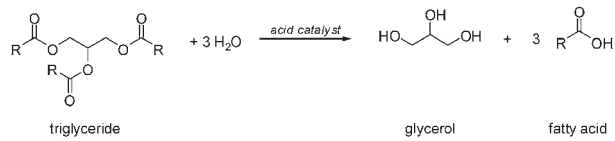
It has been established early that acids catalyze this hydrolysis reaction, thus liquid sulfuric acid has been used. Heterogeneous catalysis can potentially provide simpler and environmentally more benign processes, however, *via* ease of separation and recovery. Thus, solid acids, such as acidic ion-exchange resins,[65,66] zeolites and heteropolyacids, can replace the homogeneous acids. Hydrolysis of sucrose is in fact already established on an industrial scale using acid ion-exchangers,[67] but the main route is still *via* enzyme catalysis. Transfer to the heterogeneous system shows problems regarding the microenvironment of the swollen polymer, *i.e.* limitation of diffusion and restricted accessibility, as well as the production of many by-products.[68]

In an effort to make this switch to heterogeneous catalysts viable, various acidic exchange resins have been tested, including those prepared by radiation-induced grafting to produce graft copolymers capable of hosting sulfonic groups.[69–71] A common problem with solid acids, including ion-exchange resins, is that they are subject to poisoning by water. Thus, sulfonated mesoporous silicas were investigated as a new class of solid acids, giving glucose and fructose in 90% yield after four hours at 80 °C.[72] Zeolites are also acid ion-exchangers. A conversion of sucrose of up to 90% with close to 90% selectivity and very few by-products formed was achieved using highly dealuminated zeolite Y at 70 °C.[73] Similarly, the activity of various dealuminated zeolites was compared, again showing high selectivities and few by-products, regardless of the conversion.[74] Similarly, the hydrolysis of maltose was studied by comparing the performance of acid zeolites, ion-exchange resins, amorphous silic-aluminas and also the ordered mesoporous material, MCM-41.[75] The best results were achieved with zeolite beta (Si/Al = 50) at 130 °C and 10 bar where a conversion of 85% and a selectivity of 94% was reported. Most recently, the use of organic–inorganic hybrid mesoporous silica catalysts was reported for the hydrolysis of cellubiose to yield glucose. Cellubiose was used as a model for oligosaccharides, and it was possible to achieve 100% conversion at 175 °C but significant glucose degradation was observed simultaneously.[76]

It can be seen then that heterogeneous catalysis may find an opportunity for replacing the enzymatic catalysis of disaccharides to its monosaccharides, and thereby provide industry with a more efficient and benign route. However, it is also clear that more selective catalysts are required.

4.2.2 Triglycerides. Triglycerides can be hydrolyzed to give fatty acids and glycerol (Scheme 2). The fatty acids obtained have many industrial uses, mostly

for the manufacture of soap. Glycerol is currently viewed as a by-product from this reaction, but maybe in the future it will be considered a commodity due to the current drive to develop it as a feedstock. Technologies in this area have often featured high temperatures and pressures because of low reaction rates. In an attempt to develop low temperature and pressure processes, as well as methods that are easy to implement, heterogeneous catalysis has been pursued as an alternative.



Scheme 2 Triglycerides can be hydrolyzed to give fatty acids and glycerol. This can be catalyzed by solid acid catalysts like zeolites or acid exchanged resins.

Similarly to the hydrolysis of sucrose, acid exchanged resins can be utilized, in one case to give 75% hydrolysis of triglycerides after six hours at 155 °C. It was shown that the Brøndsted acid sites catalyze the hydrolysis reaction, which was performed in the liquid phase with continuous steam injection.[77] The same authors reported that polystyrene sulfonic cation-exchange resin, loaded with 13% of the superacid H_3Mo, gave 74.5% hydrolysis of palm oil at 155 °C in a batch reactor also operated with steam injection.[78]

4.2.3 Polysaccharides. Before the introduction of enzymes (α-amylase and glycoamylase) to facilitate the hydrolysis of polysaccharides, this transformation was typically achieved using strong mineral acids. There have also been studies of the use of ion-exchange resins and of the zeolite mordenite to catalyze the hydrolysis of amylose and starch at 130 °C and 10 atm. With the ion-exchange resin, it was seen that the selectivity towards glucose was not lowered by lengthening the reaction time. However, this was not the case for mordenite where substantial degradation of the glucose was observed.[75] With the ion-exchange resin, it was possible to obtain 35% glucose after 24 hours reaction time. Similarly, the performance of an ion-exchange resin (Amberlyst 15), nafion-silica and sulfonated mesoporous silicas were compared for starch hydrolysis. The best yields reported were 39% glucose and 18% maltose obtained at 130 °C.[79]

5. Catalytic dehydrations

5.1 Introduction

There are several examples of dehydrations of chemicals derived by renewable resources by use of heteregeneous catalytic approaches in the literature. These can be categorized into three types of reactions: (a) reactions in which one (or more) molecule(s) of water is eliminated from a single substrate molecule, (b) reactions in which one (or more) molecule(s) of water is generated as the result of an esterification reaction between an alcohol and a carboxylic acid or carboxylic acid derivative and (c) reactions in which one (or more) molecule(s) of water is generated due to an etherification reaction between two alcohol functionalities.

5.2 Dehydration reactions involving bio-resources and primary renewable building blocks

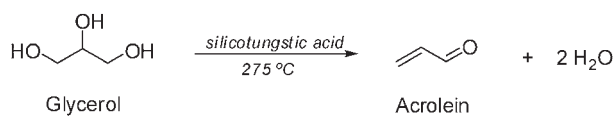
5.2.1 Bio-oils. Transesterification of vegetable oils to produce fatty acid methyl esters (FAME) which can be used as biodiesel has been studied intensely in recent years. Mainly solid bases such as MgO and hydrotalcites are used as catalysts,[80,81] however, solid acids are also studied for these reactions.[81] In a study with soybean oil as the source of fatty acids, MgO catalysts prepared in different ways, as well as a hydrotalcite catalyst, were all

reported to be effective catalysts for the transesterification reactions yielding between 75 and 95% FAME after 1 h at 180 °C, whereas application of alumina resulted in less than 5% FAME.[80] At 200 °C, all the tested base catalysts (except one of the four MgO ones) resulted in a yield of FAME of 95–100%. In a similar study, experiments carried out at 180 °C showed a difference in the yields obtained using hydrotalcite and MgO catalysts.[81] Using hydrotalcite, 92% yield was obtained, whereas the yield using MgO was 75%. However, the yield obtained using these catalysts were similar (75–80%) when the reaction mixture also contained some free fatty acid. In this study, pure and metal-substituted vanadyl phosphates (MeVPO) as well as titanated silica (tetraisopropoxide titanium grafted onto silica) were also tested for the reaction.[81] The best results were obtained with GaVPO with which a yield of 82% FAME yield was obtained. The transesterification reactions have also been studied using alumina-supported solid base catalysts at methanol reflux temperatures, *e.g.* using catalysts made by calcining KNO_3 adsorbed on Al_2O_3.[82] The study showed that 35 wt% KNO_3/Al_2O_3 calcined at 500 °C was the optimum catalyst for the reaction, and this catalyst gave 87% yield after a reaction time of 7 h. Recently, KF/Al_2O_3 has also been reported as catalyst for transesterification at about 65 °C in a study using cottonseed oil as the fatty acid source,[83] and even poultry fat has been transesterified recently using hydrotalcite as the catalyst.[84]

5.2.2 Syngas and methanol. Methanol is one of the top industrial chemicals today. It is produced on a very large scale from fossil-derived syngas by use of a Cu–Zn–Al-oxide catalyst, however, it can of course also be produced in a similar manner from bio-derived syngas. Methanol (and also syngas) can be used as a feedstock to produce dimethyl ether *via* catalytic dehydration. However, the chemistry involved in these processes is well-known, and will not be considered here, since it has been extensively dealt with in detail elsewhere.[85–87]

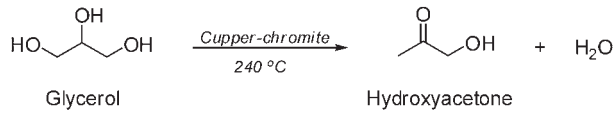
5.2.3 Ethanol. Ethanol is the most important chemical produced by fermentation, and it has the potential to become a major feedstock for the chemical industry since many other large-scale chemicals can be produced from ethanol. In fact, ethanol can in many respects be considered a renewable alternative to ethylene, which is the largest volume carbon-containing chemical produced from fossil resources today. *Via* catalytic dehydration, ethanol can easily be converted into ethylene and diethyl ether, both of which are well-known acid catalyzed processes. Almost all available solid dehydration catalysts have been tested for these reactions, and a comprehensive review of this field is beyond the scope of this review. The reader is referred elsewhere for reviews on these topics.[88–91]

5.2.4 Glycerol. It has long been known that glycerol can be dehydrated to produce acrolein by heating aqueous glycerol with a mixture of finely powdered $KHSO_4$ and K_2SO_4 (Scheme 3).[92] Recently, the reaction has received attention again, as several acidic solid oxide catalysts were tested as catalysts for the reaction.[93–95] The best results were obtained with silica-supported heteropolyacids such as silicotungstic acid with which 86% selectivity towards acrolein was obtained at 98% conversion of glycerol at 275 °C.[93] Also tungstated zirconia has been reported to be a selective catalyst for acrolein formation in a comparative study of many different catalysts; using 15 wt% WO_3/ZrO_2, 65% selectivity towards acrolein was achieved at 100% conversion at 325 °C.[95]



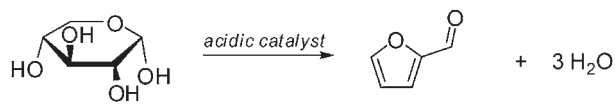
Scheme 3 Acrolein can be obtained by dehydration of glycerol. The reaction was reported many years ago using powdered $KHSO_4/K_2SO_4$ as catalyst. Recently, the use of silica-supported heteropolyacids has also been described, notably with silicotungstic acid as catalyst.

Another dehydration product from glycerol is hydroxyacetone, or acetol (Scheme 4). In one study, several catalysts were tested for this reaction.[96] Of the tested catalysts, however, only copper-chromite appeared to be effective for this transformation. Using this catalyst, 80% selectivity towards hydroxyacetone was achieved at 86% conversion in a reactive distillation experiment carried out under a slight vacuum (98 kPa) at 240 °C.[96]



Scheme 4 Hydroxyacetone can be obtained from glycerol by dehydration. The reaction has been reported using copper–chromite as catalyst.

5.2.5 Xylose. Catalytic dehydration of xylose, which is the most abundantly available pentose monomer in hemicellulose, has been known for a long time (Scheme 5). In fact, as early as 1922, an industrial process involving sulfuric acid catalyzed dehydration of xylose to produce furfural was developed by the Quaker Oats Co.

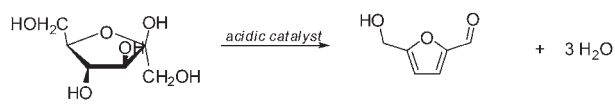


Scheme 5 Xylose can be dehydrated to produce furfural. The reaction has been reported using several different catalysts including zeolites, sulfonic acid functionalized MCM-41 and immobilized heteropolyacids. The best selectivity towards furfural was achieved using zeolite H-mordenite, although at low conversion of xylose.[88] Overall, the best yield of furfural was obtained using sulfonic acid functionalized MCM-41.

Recently, several reports concerning this reaction have appeared in literature describing the use of zeolites,[97] ion-exchange resins,[98] sulfonic acid functionalized MCM-41,[98] immobilized heteropolyacids,[99–101] niobium silicates[102] and exfoliated titanate and niobate nanosheet structures[103] as solid acid catalysts. In 1998, Moreau *et al*. compared zeolites H–Y and H-Mordenite in batch experiments at 170 °C with 1 : 3 water/toluene or water/methyl isobutylketone mixtures as the reaction media. It was found that H–Y was generally the most active catalyst whereas H-mordenite was the most selective towards furfural formation; up to 96% selectivity at 27% conversion after 30 min. using water/toluene as the reaction media.[97] Using sulfonic acid-functionalized MCM-41, 82% selectivity at 91% conversion was achieved after 24 h at 140 °C using either DMSO or toluene/water as the extraction phase.[98] Under the same conditions, application of Amberlyst-15 resulted in only 70% selectivity towards furfural at 90% conversion. Catalysts made by functionalizing MCM-41 with heteropolyacids have also been tested for the reaction. In general, however, the performances of these catalysts are not particularly good, as the highest selectivity achieved in a study of several heteropolyacids using different extraction phases were 67% at 94% conversion after 4 h at 140 °C.[99] Moreover, microporous AM-11 niobium silicate and ordered mesoporous niobium silicates have been reported as catalysts for dehydration of xylose, however, at 160 °C no more than 56% selectivity at 89% conversion was obtained using microporous AM-11.[102] However, the study also showed that the reaction temperature could be raised to 180 °C whereby the

furfural yield increased from *ca.* 20% after 1 h at 160 °C to *ca.* 45%. Very recently, exfoliated and acidified layered titanates, niobates and titanoniobates prepared by heating mixtures of TiO_2 or Nb_2O_5 with alkali carbonates followed by immersion in aqueous HCl or HNO_3 and finally exfoliating the sheets with tetrabutylammonium hydroxide.[103] Using these catalysts, furfural yields up to 55% could be obtained at 92% conversion after 4 h at 160 °C.

5.2.6 Glucose and fructose. Sucrose is one of the largest chemicals readily available from biomass. It is produced from sugar cane or sugar beats and can be easily hydrolyzed into its constituent monomers, glucose and fructose. In general, dehydration of these carbohydrates will lead to the formation of many different products, however, some control of the dehydration products obtained can be achieved using different acid catalysts. The target chemical in most reports concerning solid acid catalyzed dehydration of hexoses is 5-hydroxymethyl furfural (Scheme 6), and to a lesser extent levulinic acid, which is formed along with formic acid from HMF by a rehydration–decomposition reaction. HMF is sometimes referred to as a "sleeping giant" due to its enormous potential importance as a key chemical intermediate,[104] and several reviews are available concerning the production as well as chemistry of HMF.[105,106] Very recently, significant achievements were made in the production of HMF by homogeneous catalytic approaches.[107] Typically, the starting material for HMF synthesis is fructose, however, there exists, of course, great interest in establishing a commercially viable process directly from glucose, since glucose is less expensive than fructose. Several types of catalysts have been applied for dehydration of fructose to produce HMF. These were categorized into five classes of catalysts (organic acids, inorganic acids, salts, Lewis acids and other) by Cottier *et al.* who also categorized the different methods by which the dehydration reaction was carried out into five different types (aqueous media below 100 °C, aqueous media above 100 °C, non-aqueous media, mixed-solvent systems and solvent-free/microwave processes).[105] Most of the solid acids applied in the synthesis of HMF from fructose, zeolites, ion-exchange resins, solid inorganic phosphates, belong to the group of "other catalysts" according to the categorization of Cottier *et al.* Although levulinic acid can be an interesting target in itself, it is nonetheless an undesirable byproduct in processes targeting HMF, particularly, when water is used as the reaction media. Therefore, the most successful approaches to circumvent levulinic acid formation by HMF rehydration–decomposition is to carry out the reaction in a mixed water-organic solvent system, so that HMF is removed from the aqueous phase as it forms. Literature covering the synthesis of levulinic acid can be found in section 5.3.



Fructose 5-hydroxymethyl furfural

Scheme 6 Fructose can be transformed into 5-hydroxymethyl furfural (HMF) *via* acid-catalyzed dehydration. Solid acid catalysts applied to facilitate the reaction are zeolites, ion-exchange resins and solid inorganic phosphates. With sporadic success, notably with inorganic phosphates, other carbohydrate sources such as inulin can also be transformed into HMF.

With zeolites as the solid acid catalyst, the best results for HMF synthesis were obtained by Moreau *et al.* who tested acidic mordenites with different Si/Al ratios in batch experiments and reported that dealuminated H-Mordenite with Si/Al ratio of 11 exhibited the highest selectivity and even so at reasonably high fructose conversion (91% selectivity at 76% conversion after 60 min. at 165 °C using water/methyl isobutyl ketone as the reaction media).[108] Other zeolites, H-Y, H-Beta and H-ZSM-5

were also tested for the reaction, however, none of these catalysts were as selective as H-mordenite.[109]

Also acidic ion-exchange resins were tested as catalysts for fructose dehydration. Using PK-216, a solution of water-DMSO-polyvinylpyrrolidone containing 10 wt% fructose was dehydrated to HMF after 8–16 h at 90 °C with 71% selectivity at 80% conversion using MIBK as the extraction phase.[107] Using a more concentrated fructose solution (30 wt%), 65% selectivity was achieved at 83% conversion. Working in more dilute solution (0.5 M in DMSO), also with PK-216 as the catalyst, an HMF yield of 90% was obtained after 5 h at 80 °C.[110] Even more remarkable perhaps was the observation that the reaction could be carried out in a continuous process with no signs of deactivation even after 900 h, in this case using Amberlite IR-118 as the catalyst. Recently, Amberlyst 15 was also reported as catalyst for fructose dehydration to produce HMF at 80 °C using a solvent system comprising DMSO and either a hydrophilic (BMIM-BF_4) or hydrophobic (BMIM-PF_6) ionic liquid.[111] In both cases, HMF yields of *ca.* 80% were achieved after 24 h, however, when the reaction was carried out without DMSO as co-solvent, a maximum yield of only *ca.* 50% yield could be achieved (after 3 h) using BMIM-BF_4. Very recently, ionic liquids immobilized on silica (ILIS) were used as catalysts for dehydration of fructose to HMF.[112] In the study, it was shown that both Lewis and Brøndsted acidic ILIS were effective for the transformation. 70% yield was obtained at 100% conversion after 4 min. of 200 W microwave irradiation in DMSO using Brøndsted acidic 3-allyl-1-(4-sulfobutyl)imidazolium trifluormethanesulfonate [ASBI][Tf], whereas a yield of 67% was achieved using Lewis acidic 3-allyl-1-(4-sulfurylchloride butyl)imidazolium trifluormethanesulfonate [ASCBI][Tf].

A third class of solids, which were tested as catalysts for carbohydrate dehydrations are inorganic phosphates. In a comparative study including vanadyl phosphate ($VOPO_4 \cdot 2H_2O$) and partially metal-substituted vanadyl phosphates ($M_xVO_{1-x}PO_4 \cdot 2H_2O$, M being Cr, Mn, Fe, Al and Ga), it was shown that vanadyl phosphate, which contains both Brøndsted and Lewis acid sites, is very selective towards HMF formation (80% selectivity at 50% conversion after 1 h) under mild conditions (80 °C) and in pure water.[113] Moreover, it was shown that partial Fe-doping increased the performance quite significantly, so that even at very high fructose concentrations, a reasonable yield of HMF could be achieved (84% selectivity at 71% conversion using 30 wt% fructose as the reaction media). The study also showed that the catalyst performances are very similar when inulin is used as the carbohydrate source in stead of fructose, perhaps opening up the possibility of producing HMF from an even more inexpensive source than fructose. Overall, the performance of the vanadyl phosphate catalysts at 80 °C was quite similar to the performance of zirconium and titanium phosphate and pyrophosphate catalysts operated at 100 °C. Of the latter two types of catalysts, the best performance was achieved with cubic zirconium pyrophosphate and γ-titanium phosphate, that gave selectivities of up to 99.8% and 98.3% after 30 min., respectively.[114] Also selectivities up to *ca.* 100% were reported for niobium phosphate systems at 100 °C, although at low conversions of fructose.[115,116] Very recently, niobic acid and niobium phosphate catalysts were also studied under continuous flow conditions in aqueous medium. It was shown that the niobium phosphate catalyst was more active than the niobic acid catalyst due to it having a more acidic surface.[117] The use of zirconium phosphates under subcritical water conditions was also reported recently. In the study, it was shown that HMF yield of 61% at 80% fructose conversion could be achieved after only 2 min. at 240 °C.[118] Using glucose as the reactant under otherwise similar conditions, only 39% selectivity was achieved.

Dehydration of glucose and fructose was also reported using solid oxide catalysts. With anatase-TiO_2 (a-TiO_2) and a mixture of monoclinic and tetragonal ZrO_2 (m/c-ZrO_2) it was reported that fructose could be relatively selectively dehydrated to HMF after only 5 min. at 200 °C, although in quite low yields (*ca.* 25%).[119,120] With

the same catalysts but with glucose as the starting material, a-TiO_2 was much more selective towards HMF than m/c-ZrO_2, which gave more or less the equilibrium mixture of 1,6-anhydroglucose and HMF, which was also obtained in the absence of a catalyst. However, it should be noted that m/c-ZrO_2 presumably catalyzes the isomerization of glucose into fructose since more than 60 mol% fructose was present in the reaction mixture after experiments starting from aqueous glucose.

In 2000, Kröger *et al.* reported that 2,5-furan-dicarboxylic acid (FDCA) could be produced in a combined one pot dehydration–oxidation reaction starting from fructose, however, only in 25% yield.[121] Very recently, this was improved significantly, when Ribeiro and Schuchardt reported that also SiO_2-gel containing $Co(acac)_3$ could be used as catalyst for the combined dehydration–oxidation reaction of fructose to yield FDCA.[122] With pure SiO_2-gel, *ca.* 100% HMF selectivity could be achieved at *ca.* 50% conversion after 65 min. at 160 °C. However, with $Co(acac)_3$ encapsulated in SiO_2-gel, a 70% one-pot yield of 2,5-furan-dicarboxylic acid was achieved. This proves an important point, namely that an alternative strategy to improving the HMF yield by adding an extraction phase is simply to react it further *in situ* to desired end-products.

5.3 Dehydration reactions involving commodity chemicals

5.3.1 1,2- and 1,3-Propanediols. Dehydration of 1,2- and 1,3-propanediols to produce allyl alcohol was studied using CeO_2 as the catalyst.[123,124] With 1,3-propanediol, the reaction is very specific towards allyl alcohol which is formed with 99% selectivity at 51% conversion at 325 °C.[123] At the same temperature and with 1,2-propanediol as the substrate, only 44% selectivity was achieved and at very low conversion. At elevated temperatures, higher conversion of 1,3-propanediol can be achieved, however, at a substantial drop in selectivity. At 425 °C, the selectivity towards allyl alcohol was 54% at 78% conversion of 1,3-propanediol.

5.3.2 Succinic acid. Succinic acid is also available *via* fermentation of glucose, and has the potential to become a large-scale industrial chemical in the future. However, there are only a few reports on dehydration reactions involving succinic acids in the literature, and most of these are concerned with esterification to produce dialkyl esters. The synthesis of various dialkyl esters was reported using metal exchanged montmorillonite clays (Na^+, Mn^{2+}, Zn^{2+}, Ni^{2+}, Cr^{3+}, Fe^{3+} and Al^{3+}) as the catalysts.[125–127] For dimethyl succinate, 70% isolated yield was achieved using Fe^{3+}-exchanged montmorillonite after 4.5 h at methanol reflux temperature.[127] For dibutyl succinate, the best results were obtained with Al-montmorillonite (94% yield after 8 h, also at reflux temperature), which also proved to be a good catalyst for other esterification reactions, *e.g.* for diesterification with isobutyl alcohol to produce di-(isobutyl) succinate in 98% yield.[126] Very recently, a new family of materials known as Starbons was also applied for esterification of succinic acid with ethanol in aqueous ethanol solution.[128,129] Using sulfonated Starbon-400-SO_3H as the catalyst, diethyl succinate was obtained in >99% after *ca.* 9 h at 80 °C.[128]

5.3.3 Levulinic acid and itaconic acid. Levulinic acid could also become an important intermediate chemical in the future since it can be produced by acid catalyzed dehydration–decomposition of fructose. The synthesis of diethyl levulinate was recently reported using sulfonated Starbon-400-SO_3H. The selectivity towards the diester was >99% at 85% conversion after 6 h at 80 °C.[128] In the paper esterification of itaconic acid was also reported. However, this reaction is much slower and less selective, as ethyl itaconate was achieved with 75% selectivity at 81% conversion after 24 h.[128]

5.3.4 Sorbitol. Sorbitol is the sugar alcohol obtained by reduction of glucose and it can be dehydrated to either isosorbide or to 1,4- and 2,5-sorbitan in acid or base catalyzed processes, respectively. Using sulfonic acid functionalized MCM-41 type materials lauric acid esters of isosorbide can be achieved quite selectively starting from sorbitol (>95% selectivity towards isosorbide dilaurate at 33% lauric acid conversion) in a dehydration–esterification reaction.[130]

6. Catalytic oxidations

6.1 Introduction

Oxidation as a process to transform biomass into value-added chemicals is a key one. Here, we focus on oxidations using molecular oxygen as the oxidant, with the aim of illustrating selected interesting reactions that could be important in the efforts to develop sustainable chemistry since they only require abundant bio-resources as reactants and have water as the only, or at least the main, byproduct.

6.2 Oxidation reactions involving primary renewable building blocks

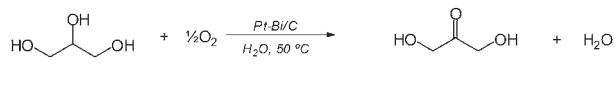
6.2.1 Ethanol. Acetic acid, an important chemical reagent and industrial chemical with a global demand of around 10 million tonnes per year, can be produced from the oxidation of bioethanol. It has a very large number of industrial applications *e.g.*, in the production of cellulose acetate for photographic films and in polyvinyl acetate for wood glue. Moreover, it also finds use in the food industry as an acidity regulator, as the additive E260.

The oxidation of ethanol to acetic acid was among the first heterogeneous catalyzed reactions to be reported, but it has not attracted continued interest. During the 1990ies, however, 100% conversion of ethanol coupled with 100% selectivity to acetic acid was reported in a gas-phase reaction using molybdenum oxide catalytic systems on various supports, at temperatures below 250 °C.[131] Similarly, a tin oxide and molybdenum oxide catalyst was used with a feed consisting of 80% aqueous ethanol to produce acetic acid at 320 °C.[132] Recently, it was reported that a mixed Mo-V-Nb oxide also catalyzes the selective oxidation of ethanol to acetic acid with oxygen in a gas phase reaction at about 235 °C with 95% selectivity at full conversion at about 235 °C.[133]

At even milder conditions, gold nanoparticles were found to be effective heterogeneous catalysts for this reaction in aqueous phase. A yield of acetic acid of 92% after eight hours and at the considerably lower temperature of 180 °C and 3.5 MPa air pressure was achieved, employing $Au/MgAl_2O_4$ as the catalyst, and starting from ethanol concentrations comparable to those obtained by fermentation (*ca.* 5 wt% aqueous ethanol). Platinum and palladium, as traditional catalysts in this area, were compared to gold to show that a superior selectivity and conversion can be achieved using gold catalysis. At 180 °C, 3 MPa air pressure and after four hours, gold yielded 83% acetic acid, platinum 16% and palladium 60%. Moreover, gold catalysts exhibited a selectivity of 97%, whereas platinum and palladium gave only 82% and 93%, respectively.[134] At higher ethanol concentrations (above 60%), the same catalytic reaction leads primarily to formation of ethyl acetate[135] and the reaction was shown to proceed *via* acetalaldehyde as intermediate.

6.2.2 Glycerol. Recently, the possibilities for oxidizing glycerol into valuable chemicals have received significant attention, and there are several recent reviews with entire sections devoted to this particular topic.[136–138] The market for glycerol oxidation products is not yet developed due to the current catalytic routes providing too low selectivities and yields. However, since many expect that glycerol will be widely (and inexpensively) available as a result of glycerol being a major waste product in the production of biodiesel by transesterification,[136] there is a significant drive to

develop new catalytic technologies. Glycerol possesses two (identical) primary alcohol functionalities and one secondary. Consequently, there exist a multitude of possible products from the oxidation reaction. Catalytic selectivity is therefore a central factor to consider in developing this chemistry. In fact, the nature of the metal, as well as the pH, largely controls the selectivity for converting either type of alcohol. The main products possible from glycerol oxidation are glyceric acid or glycerate depending on pH, dihydroxyacetone (DHA), and glyceraldehyde. Under acidic conditions, oxidation of glycerol usually leads to the formation of DHA (Scheme 7). In initial experiments performed at pH of 2–4, platinum on charcoal showed low catalytic activity for oxidation of the secondary hydroxy group of glycerol with a dihydroxyacetone yield of only 4% at a glycerol conversion of 37%. Several promoters were tried, including bismuth, tellurium, lead, tin, and selenium. On addition of bismuth (mass ratio of bismuth/platinum = 0.2), a drastic increase was seen in the DHA selectivity, which increased from 10% to 80%.[139] The bismuth addition decreases the conversion slightly, but the yield still increased from 4% to 20%.

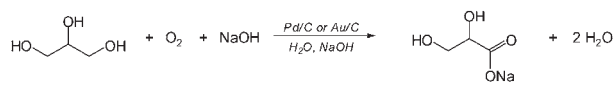


glycerol dihydroxy acetone

Scheme 7 Oxidation of glycerol in acid media leads to dihydroxyacetone, using Pt–Bi/C as catalyst.

The selective oxidation of a 50% aqueous solution of glycerol was performed at 50 °C with an oxygen/glycerol ratio of 2, in a continuous fixed bed process using a Pt–Bi catalyst supported on charcoal. Here, a DHA selectivity of 80% at a conversion of 80% was obtained.[140]

Under basic conditions, oxidation of glycerol mainly leads to the formation of glycerate (Scheme 8). By employing a 5 wt% Pd/C catalyst, the selectivity to glycerate can be as high as 70% at 100% conversion at pH = 11.[141,142]

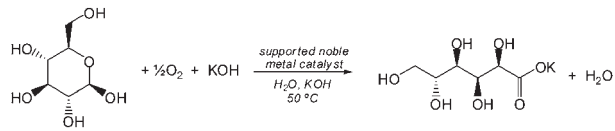


glycerol sodium glycerate

Scheme 8 Oxidation of glycerol in basic media leads to glyceric acid, using Pd/C or Au/C as catalyst.

During the last few years, significant attention has been devoted to the aerobic oxidation of glycerol using heterogeneous gold catalysts. Glycerol was oxidized to glycerate in the presence of NaOH with 100% selectivity at 60 °C using water as the solvent, and at an oxygen pressure of 0.3 MPa. The catalysts used were either 1% Au/charcoal or 1% Au/graphite both giving around 55% conversion.[143] A range of different supports for the gold nanoparticles catalysts were investigated, TiO_2, MgO, and Al_2O_3, but all showed low activity compared to Au/C. Depending on the base concentration and the reaction time, the selectivity of the Au/C catalyzed liquid phase glycerol oxidation could be controlled.[144] Most recently, it was shown that hydrogen peroxide is formed during oxidation of glycerol using gold catalysts[145] and that this leads to C–C bond breakage and a resulting loss of selectivity. This was independently supported by the fact the Au–Pd catalysts showed higher selectivity to glycerate than the monometallic Au catalyst, which was shown to be related to the higher efficiency of Pd to catalytically decompose the produced hydrogen peroxide *in situ*.[146] By employing a reaction temperature of 100 °C and an air pressure of 21 bar with methanol as the solvent, it is possible to obtain dimethyl mesoxalate in yields as high as 89%[147] and this clearly illustrates the effect of temperature on the degree of oxidation of the glycerol feedstock.

6.2.3 Glucose. Glucose can be selectively oxidized to a number of products. Currently, gluconic acid, glucuronic acid, glucaric acid and 2-keto-gluconic acid can be formed from such catalytic transformations. All these oxidations can be performed with air or oxygen, in an aqueous medium, under mild conditions and using a supported noble metal catalyst. Owing to the multifunctionality of glucose, the possibility of controlling the catalytic selectivity is again highly important. By use of Pt/C as the catalyst, the anomeric carbon atom of glucose is oxidized most readily, followed by the terminal primary alcohol moiety. The least oxidizable group is found to be the equatorial alcohol moieties.[148–150] A plausible mechanism of the reaction is that a dehydrogenation of glucose takes place to form gluconic acid and adsorbed hydrogen on the platinum surface. The hydrogen is then subsequently oxidized by oxygen to form water. This mechanism is supported by the observation that gluconic acid is formed even in the absence of oxygen in strongly basic solution and in the presence of the Pt catalyst.[148,149] The main product from the reaction of glucose is gluconic acid (Scheme 9). This represents one of the first examples where oxidation occurs solely by dehydrogenation, and thus it is clearly an attractive option with the only reagents required being simply water and hydroxide ions.[151,152]



glucose gluconic acid

Scheme 9 Oxidation of glucose to gluconic acid has been reported using oxidation catalysts such as Pt/C, Pd/C, Pd–Bi/C and Au/C.

Gluconic acid is found naturally in many fruits, in tea and in wine. Gluconic acid is also used as an additive, to regulate pH in food (E574). Currently, gluconic acid is produced industrially from glucose, using glucose oxidase enzymes. The market of gluconic acid is in the range of 60.000 t/year.[153] However, heterogeneous catalytic oxidation is also a viable method, and one under currently intense investigation. It has been debated whether the currently best heterogeneously catalyzed process is possibly better than the industrial biocatalytic process.[154]

Oxidation is usually selective for the anomeric position, as mentioned previously. Thus when glucose is oxidized in the presence of supported metal catalysts, specifically Pd and Pt, gluconic acid is achieved in high yields, for example with 5% Pt/C, a 70% yield is obtained,[155] or, also reported, complete conversion is seen with Pd/C after six hours.[156] However, when using palladium catalysts deactivation is observed at high conversions. This problem can be alleviated using a modified palladium catalyst. Thus, a Pd–Bi/C catalyst was found to be capable of oxidizing glucose to gluconic acid with excellent selectivity (95–100%) at rates up to 20 times greater than that of the Pd/C catalyst.[157,158] An oxidative dehydrogenation mechanism is also proposed here.[159]

The use of gold as a catalyst in the oxidation of glucose to gluconic acid has also been reported, on supports such as activated carbon, CeO_2, TiO_2, Fe_2O_3. Gold exhibits somewhat lower selectivity than the Pd-Bi/C catalyst, though. However, the activity of gold is strongly dependent on particle size, and it is less sensitive to low pH, being active even under acidic conditions.[160–164] In the aerobic oxidation of glucose over gold catalysts, hydrogen peroxide has been observed to be a reaction product, just as it was the case in the oxidation of glycerol.[165] Most recently, it has proved possible to achieve long-term stability (recycled 17 times without noticeable loss of activity) of an Au/TiO_2 catalyst in the oxidation of glucose at pH = 9, and at temperature between 40 and 60 °C.[166]

6.3 Oxidation reactions involving commodity chemicals

6.3.1 1,2-Propanediol and 1,3-Propanediol. 1,2-propanediol and 1,3-propanediol can be obtained as hydrogenation products of glycerol. The first example of gold catalysts being able conduct aerobic oxidations of alcohols was provided by Prati and Rossi, who showed that 1,2-propanediol can be oxidized at about 80 °C in alkaline aqueous solution to yield lactate with a selectivity of 90–100% at 80–94% conversion using an Au/C catalyst.[167] Later, it was shown that similar results can be achieved using Au nanosols stabilized with poly(vinylalcohol).[168] If the reaction is instead performed in methanol, it is only necessary to add a catalytic amount of base, and under these conditions 1,2-propanediol and 1,3-propanediol are oxidized to yield methyl lactate and methyl-3-hydroxypropionate, respectively. Methyl lactate can be formed with 71% selectivity at 99% conversion in the presence of 2 wt% Au/TiO_2. The reaction requires about 20 hours at 100 °C and with 2.5 MPa air pressure.[147] Similarly, methyl 3-hydroxypropionate can be produced with a somewhat higher selectivity of 85% at 99% conversion.[147]

6.3.2 Acrolein. Acrylic acid and acrylate esters constitute an important group of chemicals in today's chemical indstry, for example, they are used to make water-based paints, solvent-based coatings and acrylic coatings. Typically, acrolein is obtained by catalytic oxidation of propene. However, acrolein can also be obtained from glycerol, and in this way it can be thought considered a renewable feedstock. Industrially, acrolein is oxidized to acrylic acid in a gas-phase process operated at temperatures above 350 °C employing mixed oxide catalysts.[169] Therefore, it is noteworthy that methyl acrylate can be produced from acrolein with 87% selectivity at 97% conversion in the presence of catalytic amounts of Au/ZnO, suspended in methanol, at room temperature and ambient pressure.[170]

6.3.3 Glyceric acid. The selectivity for the catalytic oxidation of glyceric acid, and the calcium salt, can be controlled by the nature of the catalyst, and the pH, in a similar way to that of glycerol as discussed above. In this way, it is possible to obtain products corresponding to the oxidation of the primary and secondary alcohol moieties, *i.e.*, tartronic acid and hydroxypyruvic acid, respectively. As reported by Fordham *et al.*, oxidation of glyceric acid under basic conditions leads to the formation of tartronic acid whereas hydroxypuric is afforded under acidic conditions.[171] The catalyst was suspended in glyceric acid, a calcium salt added, and oxygen gas bubbled through. NaOH was added to keep the pH constant. Two catalytic systems were tested; 5 wt% Pt/C at pH 10-11 yields tartronic acid with a selectivity of 60% at a conversion of 94%; when 2% of bismuth is added, the same product is obtained but with a selectivity of 83% at 90% conversion.[171] Hydroxypyruvic acid was obtained by aerobic oxidation of glyceric acid using a bismuth-promoted platinum catalyst under acidic conditions (pH 3–4) to give a 64% yield at 75% conversion.[171] After prolonged contact with the catalyst, tartronic acid was oxidized to oxalate whereas hydroxypyruvic acid was oxidised even more rapidly to glycolic acid.

6.3.4 Lactic acid. Pyruvic acid and its derivatives are in increasing demand due to their use as precursors in the synthesis of drugs and agrochemicals.[10] It has proved difficult to obtain pyruvic acid directly from lactic acid *via* heterogeneous catalysis, because the major part of lactic acid is converted to form acetaldehyde and CO_2 by the oxidative C-C bond cleavage over most catalysts, *e.g.* V_2O_5- or MoO_3- based mixed oxide catalysts.[172]

The vapor-phase oxidation of lactic acid with air was executed using an iron phosphate catalyst with a P/Fe atomic ratio of 1.2. It was found that lactic acid is selectively converted to form pyruvic acid by oxidative dehydrogenation. The one-

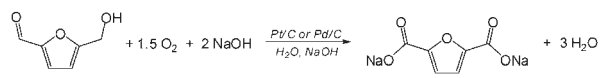
pass yield reached 50 mol%; however, acetaldehyde, acetic acid, and CO_2 was still formed, and the pyruvic acid produced decomposes over time to give acetic acid and CO_2.[173]

Oxidation has also been tried over iron phosphates with a P/Fe atomic ratios of 1.2, including $FePO_4$, $Fe_2P_2O_7$ and $Fe_3(P_2O_7)_2$, at 230 °C. The catalysts containing both Fe^{2+} and Fe^{3+} performed better than those with just one oxidation state present. The best results were 62% selectivity at 60% conversion.[174]

6.3.5 Furfural. Furfural is a commodity chemical that is readily available from dehydration of pentoses, and it can be produced in a very large scale if necessary. Furfural finds limited use today, though, which is reflected in its pricing being similar to the cheapest fossil bulk chemicals such as benzene and toluene.[10] In this way then, it can be seen that furfural could become a key feedstock in the future, especially given the new turn towards using bio-resources as a feedstock for chemicals when oil supplies become more and more insecure and/or expensive. Furoic acid is used as a feedstock in organic syntheses, and as an intermediate in the synthesis of perfumes and medicines. The oxidation of furfural to furoic acid is mainly described in patents, which discloses the use of various different catalysts including Ag_2O and Ag_2O/CuO mixtures. However, during the 1990s, the use of PbPt/C catalysts was also investigated.[175] Very recently, methyl furoate was synthesized using gold catalysis. Au/TiO_2 was suspended in a solution of furfural in methanol, a catalytic amount of sodium methoxide was added, and methyl furoate could be produced with 90% selectivity at more than 90% conversion.[176]

6.3.6 5-Hydroxymethyl furfural. 2,5-diformylfuran (DFF) is a furan derivative that has many uses, including use as a polymer building block.[177,178] By utilizing a platinum catalyst supported on carbon, and running the reaction in water at high temperatures, DFF is produced as the major product in neutral solution. If low temperatures and high pH are employed, 2,5-furandicarboxylic acid results.[179]

2,5-furandicarboxylic acid (FDCA) is another furan derivative available from oxidation of HMF (Scheme 10). It holds a great promise in the polymers industry because it can potentially replace terephthalic acid, which is produced in a massive scale for making PET plastics.[179,180] HMF is converted to FDCA under strongly alkaline conditions, pH 12 or above, with oxygen gas bubbled through the alkaline system. Platinum, or platinum and a mixture of silver and copper oxides, preferably supported on carbon, were employed as catalysts.

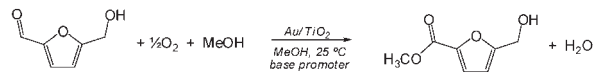


hydroxymethyl furfural — 2,5-furandicarboxylic acid

Scheme 10 Oxidation of both the aldehyde and alcohol moieties of HMF leads to formation of 2,5-furandicarboxylic acid. The oxidation reaction is catalyzed by Pt.

Oxidation of HMF was also attempted *in situ* directly from fructose, using a membrane reactor or encapsulating PtBi/C into a polymeric silicone matrix, and again, with air as the oxidant. However, the yield was never more than 25%.[181] A further attempt to obtain FDCA directly from fructose involved a one pot reaction in the presence of cobalt acetylacetonate encapsulated in sol–gel silica, at 155 °C and with 2 MPa of air pressure giving FDCA with 99% selectivity directly from fructose at a conversion of 72%.[122]

HMMF can be obtained from HMF by oxidation with Au/TiO_2 (Scheme 11), under very mild conditions—25 °C, 1 bar O_2 and 8% NaOMe—in near quantitative yields. This is an intermediate on the route to FDMC, but the reaction can be stopped at this stage.[176]



Scheme 11 Under mild conditions, oxidation of HMF in methanol can be tuned to yield methyl (5-hydroxymethyl)-furoate *via* oxidation of the aldehyde moiety.

Similarly to above, but at a higher temperature and pressure—130 °C and 4 bar O_2—2,5-furan dimethyl furoate (FDMC), a direct analogue of FDMA, can be obtained in near quantitative yields from HMF.[176] It is possible that the formation of a diester directly, rather than a diacid, could save a further synthesis step on the route to polymerization.

6.3.7 Gluconic acid. Glucaric acid can be furnished by the selective oxidation of the primary alcohol of gluconic acid with Pt-based catalysts.[182] Platinum is preferred over palladium due its greater selectivity for the oxidation of primary alcohols.[183] Low rates of oxidation of primary the alcohols is usually a complication, since products and byproducts bind more strongly to the platinum surface than the primary alcohol moiety and in effect poison the catalyst. Oxidation of secondary alcohols can also occur, leading to the formation of highly oxidized species such as oxalic acid, resulting in a poor selectivity towards gluraric acid. Gluconic acid was oxidized to glucaric acid with 55% selecticity at 97.2% conversion, using a Pt/C catalyst.[182,184]

When modifying the Pt catalyst by addition of bismuth or lead, a significant change in selectivity occurs. Oxidation of the primary terminal alcohol moiety in gluconic acid is no longer the dominating reaction. Instead oxidation of the α-hydroxy group, next to the carboxylic acid takes place, resulting in the formation of 2-keto gluconic acid with a 98% selectivity under slightly acidic conditions.[184,185] It has been proposed that the carboxylic acid coordinates to the promoter, as does the α-alcohol group, thus promoting the oxidation of the α-alcohol group.[184] This is supported by the reaction proceeding in a weakly acidic medium; when run in a basic medium, other products form and this is thought to be due to further coordination with the remaining alcohol groups.[186]

7. Catalytic hydrogenations

7.1 Introduction

Catalytic hydrogenation represents a set of reactions that will be extremely important in the production of value-added chemicals from biomass. Already now, they play a significant role in today's industry, and holds great promise for further developments. Here, selected examples of heterogeneously catalyzed hydrogenations of chemicals available from renewables resources are presented.

7.2 Hydrogenation reactions involving bio-resources and primary renewable building blocks

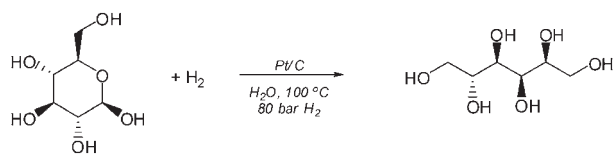
7.2.1 Cellulose. The hydrolysis of polysaccharides, *e.g.* starch, inulin, can also be combined with hydrogenation processes to yield polyols directly, in a one step process. A one-pot process was previously reported using a homogenous catalyst based on $Ru(TPPTS)_3$,[187] however, heterogeneous catalysis would be preferential in terms of the ease of recovery and re-use of the catalyst. In this way, a heterogeneous system was developed whereby ruthenium is supported on carbon, which is made acidic by treatment with different oxidizing agents, thereby catalyzing the hydrolysis part of the reaction. Selectivities to mannitol of 37–40% were achieved, which is in line with the yields from the non-coupled hydrolysis reaction, *i.e.* simply the hydrogenation reaction, from fructose to mannitol.[188] Cellulose, making up around

40–50% of biomass by weight makes it the largest component of biomass. Cellulose is a linear polysaccharide consisting of many thousands of glucose subunits. The glucose monomers are adjoined by 1-4-β glycosidic bonds, which can be hydrolysed by strong acids at high temperature. Direct hydrogenation of cellulose to sorbitol would be a highly desirable way to valorize biomass. The major complication in this strategy is the insolubility of cellulose in water. However, hydrogenation of cellulose to sorbitol has been achieved in superheated water (190 °C) using platinum and ruthenium on acidic supports.[189] The highest activity can be achieved using a 2.5% $Pt/\gamma\text{-}Al_2O_3$ catalyst which affords sorbitol in 25% yield and mannitol, resulting from epimerisation, is formed in 6% yield. The catalyst is reported to remain active after several runs. However, the maximum overall yield is limited to 31%, which is attributed to the complex structure of cellulose that does not allow it to undergo complete hydrolysis under these conditions.

In a different study, the 1-4-β glucose dimer cellubiose was used as a model substrate for cellulose. Using a polymer supported ruthenium nanocluster catalyst; cellubiose was converted to sorbitol in a one-pot hydrolysis-hydrogenation reaction in 100% yield under acidic conditions using an ionic liquid solvent.[190] This procedure was found to result in a complicated separation of the sorbitol from the ionic liquid and catalyst. A modification to the procedure was reported recently, in which cellulose is hydrolyzed in superheated water (200–250 °C) and reduced using a carbon-supported ruthenium catalyst.[191] Cellulose conversion of 85% and 39% selectivity towards hexitols (sorbitol and mannitol) was achieved with a hydrogen pressure of 60 bar using this procedure.

7.2.2 Glycerol. Hydrogenation of glycerol to 1,2-propanediol or 1,3-propanediol has been reported using different metal catalysts including nickel, copper, copper-chromite, ruthenium, rhodium palladium and platinum.[192–195] For these reactions, the difficulties lie in achieving either diol with high selectivity. One method that has proven useful for producing 1,2-propanediol selectively is to carry out the hydrogenation reaction in the presence of an ion-exchange resin in addition to a hydrogenation catalyst containing Ru.[193–196] In this approach, the ion-exchange resins functions as a dehydration catalyst which presumably facilitates the dehydration of glycerol to hydroxyacetone, that is subsequently hydrogenated into 1,2-propanediol.

7.2.3 Glucose. Catalytic hydrogenation of glucose leads to the formation of sorbitol (Scheme 12). Typically, Raney nickel is used to catalyze the reaction,[197] however, several other catalysts including platinum and ruthenium have been reported to be active for the reaction, and in many cases these catalysts are more effective than standard Raney nickel, which can be problematic due to leaching of nickel.[197–200] Very recently, an impressive yield of more than 99.5% sorbitol was obtained using Pt supported on microporous activated carbon cloth.[198] The experiments were conducted at 100 °C using a 40 wt% aqueous solution of glucose in a 300 ml stirred autoclave pressurized to a hydrogen pressure of 80 bar. The high selectivity towards sorbitol exhibited by the catalyst was attributed to fast desorption of sorbitol from the catalyst surface, which effectively lowers sorbitol epimerization and thus suppresses the formation of mannitol.



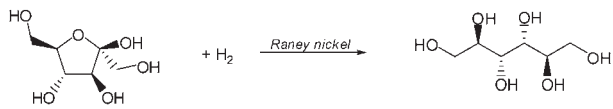
Scheme 12 Various catalysts have been applied to facilitate the catalytic hydrogenation of glucose to sorbitol, notably Pt supported on activated carbon cloth using which 99.5% yield of sorbitol can be obtained.

7.2.4 Xylose and fructose. Xylose can be hydrogenated into xylitol (Scheme 13). This reaction was reported using hydrogenation catalysts such as Raney nickel as well as platinum group metal catalysts.[201,202]

xylose xylitol

Scheme 13 Hydrogenation of xylose to produce xylitol can be achieved with 95% selectivity using Raney nickel or Ru/C as catalyst.

Raney nickel, copper and platinum group metal catalysts have also been used as catalysts for transforming fructose into mannitol *via* catalytic hydrogenation (Scheme 14).[197–199,203,204] Ruthenium supported on carbon is among the most studied catalysts for this reaction,[205] and it is, in fact, also effective for the combined hydrolysis-hydrogenation of inulin to mannitol when the carbon support has been made acidic prior to the catalytic experiments.[188] The bifunctional catalyst applied in the study was made by pre-oxidizing activated carbon (SX1G) with various oxidants such as nitric acid and ammonium persulfate and then introducing Ru onto this support by incipient wetness impregnation followed by reduction with $NaBH_4$. The oxidized carbon catalyzes the hydrolysis of inulin to a mixture of glucose and fructose which is subsequently hydrogenated to a mixture of glucitol and mannitol. Increasing the hydrogen pressure (up to 100 bar) apparently also increases the rate of hydrolysis dramatically.



fructose mannitol

Scheme 14 Hydrogenation of fructose to mannitol is catalyzed by hydrogenation catalysts such as Raney nickel and Ru/C.

7.3 Hydrogenation reactions involving commodity chemicals

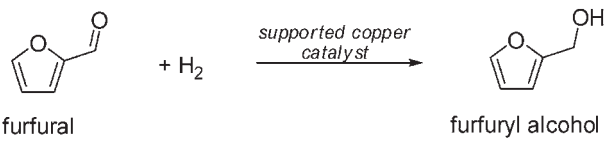
7.3.1 3-Hydroxypropanal. 3-Hydroxypropanal can be formed by fermentation of glucose and is thus an attractive starting material for production of 1,3-propanediol, which can be polymerized with *tere*-phthalic acid to produce polytrimethylene terephthalate (PTT). PTT is used in the fibers industry in the production of stain resistant carpets *etc*.

Aqueous solutions of 3-hydroxypropanal were reduced using TiO_2 supported ruthenium catalysts at 40–60 °C using 40 bar of hydrogen.[206] The most stable catalysts were found to be ruthenium catalysts supported on low surface area macroporous rutile.

7.3.2 Lactic acid. Propylene glycol (1,2-propanediol) can be employed as a de-icing agent replacing ethylene glycol, which is currently produced from fossil resources. Furthermore, propylene glycol is a safe alternative to ethylene glycol, which is toxic to humans due to its metabolism to oxalic acid.

Hydrogenation of lactic acid represents a simple route from a biomass chemical to propylene glycol. Lactic acid has been hydrogenated in the vapor phase using a Cu/SiO_2 catalyst at 140–220 °C with a hydrogen pressure of 0.1–0.72 MPa. The selectivity of 1,2-propanediol was 88% at full conversion, with 2-hydroxypropionaldehyde and propionic acid formed as the major by-products.[207] In a different study, aqueous phase hydrogenation of lactic acid was achieved using a carbon supported ruthenium catalyst. The hydrogenation is operated at temperatures from 100–170 °C with a hydrogen pressure of 7–14 MPa resulting in the formation of 1,2-propanediol in 90% selectivity at 95% conversion.[208] Disappointingly though, hydrogenation of salts of lactic acid did not result in the formation of 1,2-propandiol. Hydrogenation has also been carried out using a magnesia supported poly-γ-aminopropysiloxane-ruthenium complex in aqueous solution at 240 °C and 5 MPa hydrogen pressure for 18 hours, giving 100% yield of 1,2-propandiol, with no apparent deactivation of the catalyst.[209]

7.3.3 Furfural. Furfural is readily obtainable from dehydration of pentoses. Reduction of furfural can lead to a variety of products that are more volatile, more stable and possibly also more useful than furfural itself. Selective reduction of the aldehyde moiety leads to furfuryl alcohol (Scheme 15), whereas further reduction of the furan core will lead to tetrahydrofurfuryl alcohol. Reductive deoxygenation can result in the formation of either 2-methylfuran or 2-methyltetrahydrofuran, which can be used as liquid fuels or solvents.



Scheme 15 Hydrogenation of furfural to furfuryl alcohol is catalyzed by Cu-containing catalysts.

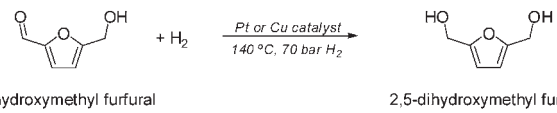
Furfuryl alcohol has traditionally been obtained from furfural by hydrogenation with copper containing catalysts, *e.g.* copper–barium–chromium oxide, copper oxide supported on silica or alumina, copper–chromium oxide and copper–cobalt oxide on silica yields furfuryl alcohol as the major product.[210] Due to its toxicity, attempts have been made to eliminate chromium from such catalytic systems, especially due to new restrictions that prevent used copper chromite catalysts from being deposited in landfill sites.[211] In recent years, several new catalytic systems have been demonstrated to successfully catalyze the hydrogenation of furfural to furfuryl alcohol. Copper has been investigated as a catalyst for this reaction on its own. Furfural hydrogenation over copper dispersed on three forms of carbon—activated carbon, diamond and graphitized fibers—was studied. Similar to other copper-containing catalysts, only products corresponding to hydrogenation of the carbonyl bond were detected, and the selectivity to furfuryl alcohol was comparable to that obtained with commercial copper chromite catalysts.[212] Copper supported on magnesium oxide has also been prepared, *via* the coprecipitation method, giving a 98% selectivity of furfuryl alcohol at 98% conversion of furfural. This is attributed to the higher number of surface copper sites and the defective sites at the copper and magnesium oxide interfacial region. Similarly, $Cu–Ca/SiO_2$ catalysts revealed a selectivity of 98% in the gas phase hydrogenation of furfural to furfuryl alcohol at a conversion of 98% and a temperature of 130 °C.[213] Various other catalytic systems have recently been used to promote hydrogenation, including a molybdenum doped cobalt-boron amorphous catalyst exhibiting excellent activity and nearly 100% selectivity to furfuryl alcohol during liquid phase hydrogenation of furfural, at 100 °C and 1 MPa hydrogen pressure.[214]

Reduction of the alcohol group to produce 2-methyl furan can be achieved using a commercial Cu/Zn/Al/Ca/Na catalyst with the atomic ratio 59 : 33 : 6 : 1 : 1. This catalyst was found to achieve 99.7% conversion with 87.0% selectivity to 2-methyl fural at 250 °C. Hydrogenation from furfuryl alcohol yields a slightly higher selectivity of 92.7% at 98.1% conversion under similar conditions.[215]

7.3.4 Levulinic acid. Hydrogenation of levulinic acid resulting in the reduction of the ketone moiety leads to 4-hydroxy pentanoic acid. This acid can cyclize to form γ-valerolactone (GVL) which is a useful industrial solvent. A 94% yield of GVL was obtained with a Raney nickel catalyst, and a hydrogen pressure of 5 MPa at a temperature of 100–150 °C.[216]

1,4-Pentanediol (PDO) holds promise for being used in the synthesis of polyesters. It has been synthesized from GVL in the presence of a copper chromite catalyst. At 150 °C and 20.3–30.4 MPa hydrogen pressure, 78.5% PDO was produced together with 8.1% 1-pentanol.[217]

7.3.5 5-Hydroxymethylfurfural. 2,5-Di(hydroxymethyl)furan can be synthesized from 5-HMF *via* hydrogenation (Scheme 16). Under a hydrogen pressure of 7 MPa at 140 °C in the presence of platinum or copper catalysts, practically quantitative yields of 2,5-di(hydroxymethyl)furan can be obtained.[218] However, under similar conditions but with palladium or nickel as catalyst, hydrogenation of the ring system occurs so that 2,5-di(hydroxymethyl)-tetrahydrofuran is obtained as the predominant product.



Scheme 16 Hydrogenation of HMF to 2,5-di(hydroxymethyl)furan is catalyzed by Pt and Cu.

8. Summary and outlook

From a chemical perspective, renewable feedstocks being highly functionalized molecules are very different from fossil feedstocks that are generally unfunctionalized. Therefore, the challenge in converting fossil resources, in particular crude oil, into useful products has been to develop methods that allow *controlled addition* of desirable chemical functionality to the hydrocarbon feedstock. Due to the quite low reactivity of the hydrocarbons; it has been possible to develop efficient catalytic processes that operate satisfactorily at relatively high temperatures and pressures. Here, heterogeneous catalysis has proven most successful and therefore played a dominant role in chemical industry. The challenge of converting renewable feedstocks into useful chemicals is very different. Still the desirable transformations are entirely dependent on catalysis, but now it is often a question of *controlled removal* of superfluous chemical functionality under sufficiently mild conditions to prevent uncontrolled degradation of the renewable feedstock. So far, most emphasis has been on using biocatalytic processes to facilitate these transformations but it appears likely that heterogeneous catalysis could also play a significant role in the future valorization of renewables. Since the conversion of bio-resources into the primary renewable building blocks is typically achieved using biocatalytic processes operating in water as the natural solvent, it seems likely that there will be a significant drive to develop heterogeneous catalysts that also operate in water, and preferably at low temperatures. In this way, it will be possible to achieve maximum process integration between the biocatalytic processes and the heterogeneously catalyzed processes. This

integration will lead to lower costs of the resulting products since the need for expensive unit operations, especially separations, will be minimized. Clearly, it represents a significant challenge to discover and develop heterogeneous catalysts that exhibit sufficient activity and selectivity under these conditions but it seems likely that this will be one of the new directions that heterogeneous catalysis will take during the next decade. The progress made in this endeavor will obviously determine how large a role heterogeneous catalysis will eventually play in the production of value-added chemicals from biomass. Here, we have shown that there are several reaction types where heterogeneous catalysis already offers some very promising opportunities but that there clearly exists a great need for further discoveries and developments in this emerging field.

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CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200800003

Unsaturated Aldehydes as Alkene Equivalents in the Diels–Alder Reaction

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Abstract: A one-pot procedure is described for using α,β-unsaturated aldehydes as olefin equivalents in the Diels–Alder reaction. The method combines the normal electron demand cycloaddition with aldehyde dienophiles and the rhodium-catalyzed decarbonylation of aldehydes to afford cyclohexenes with no electron-withdrawing substituents. In this way, the aldehyde group serves as a traceless control element to direct the cycloaddition reaction. The Diels–Alder reactions are performed in a diglyme solution in the presence of a catalytic amount of boron trifluoride etherate. Subsequent quenching of the Lewis acid, addition of 0.3% of [Rh(dppp)$_2$Cl] and heating to reflux achieves the ensuing decarbonylation to afford the product cyclohexenes. Under these conditions, acrolein, crotonaldehyde and cinnamaldehyde have been reacted with a variety of 1,3-dienes to afford cyclohexenes in overall yields between 53 and 88%. In these transformations, the three aldehydes serve as equivalents of ethylene, propylene and styrene, respectively.

Keywords: aldehydes · cycloalkenes · decarbonylation · Diels–Alder reaction · homogeneous catalysis

Introduction

The Diels–Alder reaction is one of the most powerful methods in organic chemistry for synthesis of six-membered carbocyclic compounds.[1,2] The [4+2] cycloaddition between a 1,3-diene and a dienophile gives rise functionalized cyclohexenes with good control of both regio-, enantio-, and diastereoselectivity.[2,3] The reaction has found widespread application in the synthesis of natural products and other biologically active molecules.[4,5] In the normal Diels–Alder reaction the reactivity is governed by the energy difference between the HOMO of the diene and the LUMO of the dienophile. The energy of the latter is lowered by electron-withdrawing substituents and the most common dienophiles contain carbonyl, cyano, sulfonyl or nitro groups. The effect is enhanced by coordination to Lewis acids which are known to accelerate Diels–Alder reactions substantially. For the same reason, the cycloaddition with simple olefins as dienophiles is a poor reaction which requires high temperature and pressure.[6] Instead, olefin equivalents have been developed by using electron-withdrawing groups on the dienophile that can be removed in a subsequent reduction. The most popular group is the phenylsulfonyl group,[7,8] but ethylthio,[9] nitro[10] and dichloroboryl[11] groups have also been employed. In all four cases, the Diels–Alder reaction is achieved under thermal conditions while the subsequent removal of the electron-withdrawing group is accomplished in the presence of either sodium amalgam (for $PhSO_2$),[7] Raney-Nickel (for EtS),[9] Bu_3SnH/AIBN (for NO_2),[10] or by a three-step sequence (for BCl_2) involving oxidation ($NaOH/H_2O_2$), mesylation (MsCl/pyridine) and reduction ($LiEt_3BH$).[11] However, the use of stoichiometric reducing agents for the removal of these groups diminishes the atom economy of the overall transformation. Hence, we envisioned to use α,β-unsaturated aldehydes for the Diels–Alder reaction followed by removal of the aldehyde group by a metal-catalyzed decarbonylation in the same pot. This tandem Diels–Alder decarbonylation sequence would offer a more expedient procedure for the cycloaddition with olefin equivalents and at the same time be able to maintain the regio- and stereoselectivity that characterizes the normal Diels–Alder reaction.

The catalytic decarbonylation of aldehydes can be achieved with rhodium catalysts at elevated temperatures.[12,13] The most reactive catalysts are rhodium(I) complexes containing bi- or tridentate phosphine ligands.[13] In a recent study, 1,3-bis(diphenylphosphino)propane (dppp) was shown to be the ligand of choice for this transformation among a

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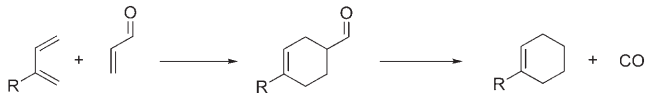
range of phosphine ligands.[14] The corresponding complex [Rh(dppp)$_2$Cl] has been used for decarbonylation of a variety of different aldehydes ranging from unprotected carbohydrates[15] to aldehydes in natural product syntheses.[16] The complex can be prepared in two steps from commercially available $RhCl_3 \cdot 3H_2O$ by conversion into [Rh(cyclooctene)$_2$Cl]$_2$ followed by ligand exchange with dppp.[17] Alternatively, the active catalyst can be generated *in situ* from the same components if the decarbonylation is performed in a diglyme solution.[14] Very recently, the mechanism for the decarbonylation was studied by experimental and theoretical methods and shown to proceed by an oxidative addition into the aldehyde C–H bond followed by a rate-limiting extrusion of carbon monoxide and reductive elimination.[18]

Herein, we describe the development of α,β-unsaturated aldehydes as alkene equivalents in the Diels–Alder reaction. Acrolein and substituted acroleins are added to various 1,3-dienes followed by a rhodium-catalyzed decarbonylation in the same pot to remove the aldehyde group (Scheme 1).



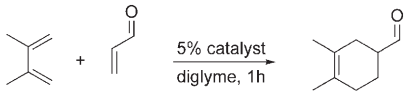
Scheme 1. One-pot Diels–Alder decarbonylation reaction.

Results and Discussion

Acrolein as dienophile: The initial experiments were carried out under thermal conditions in the presence of [Rh(dppp)$_2$Cl]. Acrolein (b.p. 53 °C) was selected as the dienophile and reacted with isoprene (b.p. 34 °C) and 2 % of [Rh(dppp)$_2$Cl] in an autoclave. The thermal Diels–Alder reaction between acrolein and simple dienes will occur at temperatures around 100 °C[19] while the catalytic decarbonylation requires a temperature around 150 °C.[14–16] Therefore, we were confident that the Diels–Alder reaction would occur before the decarbonylation. Indeed, when the autoclave was heated to 170 °C for 24 h, the reaction mixture consisted of 66 % of 1-methylcyclohexene and 34 % of the Diels–Alder adduct that had not undergone decarbonylation. Unfortunately, it was not possible to push the decarbonylation to completion under these conditions. By comparison, the decarbonylation of the same aldehyde in an open flask at 170 °C only required 4 h for full conversion. Thus, it was apparent that the liberated carbon monoxide hampered the decarbonylation in the autoclave and it was therefore decided to pursue the tandem reaction in an open system. In this case, 2,3-dimethyl-1,3-butadiene (b.p. 68 °C) was selected as the diene and reacted with acrolein at reflux. However, due to the low boiling point of acrolein, the cycloaddition required 30 h for complete conversion. More hindered dienes required even longer reaction times and this procedure was therefore not suitable for general use.

As a result, it was decided to use Lewis acid catalysis to increase the rate of the cycloaddition reaction. Several Lewis acids were selected and the reactions were investigated under neat conditions as well as in the presence of a solvent (Table 1). In the latter case, diglyme was chosen as the solvent since it had shown good results in the decarbonylation reaction.[14,15] Zinc chloride was found to be an excellent catalyst under neat conditions with full conversion in 40 min while no reaction occurred in a diglyme solution (entries 1 and 2). Furthermore, subsequent addition of [Rh(dppp)$_2$Cl] and heating to 170 °C resulted in complete decarbonylation. However, extensive isomerization of the double bond in the product also occurred, which is most likely caused by the presence of zinc chloride at elevated temperature. Thus, it appears necessary to remove or quench the Lewis acid prior to increasing the temperature in order to avoid product isomerization. Unfortunately, it was not possible to quench zinc chloride with reagents like water or ethylenediamine. Instead, a number of other Lewis acids were investigated (entries 3–8). Aluminum chloride and $BF_3 \cdot OEt_2$ gave rise to a highly exothermic reaction under neat conditions which led to instantaneous decomposition of the starting materials. In diglyme, however, the reactivity of the two Lewis acids was lowered significantly and an efficient Diels–Alder reaction could be achieved with the latter. The cycloaddition went to completion in 10 min at room temperature with 5 % of $BF_3 \cdot OEt_2$ and afforded the product in 89 % isolated yield. The conversion with aluminum chloride and other Lewis acids were slower.

Table 1. Diels–Alder reaction with acrolein catalyzed by various Lewis acids.[a]



Entry	Catalyst	Conversion of diene [%][b]
1	$ZnCl_2$	0
2[c]	$ZnCl_2$	>99
3	$AlCl_3$	43
4[d]	$BF_3 \cdot OEt_2$	>99
5[e]	$FeCl_3$	37
6	$La(OTf)_3$	0
7	$Sc(OTf)_3$	66
8	$Bi(OTf)_3$	75

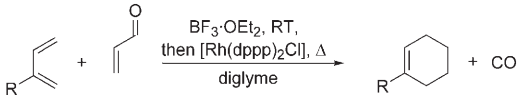
[a] To a solution of 2,3-dimethyl-1,3-butadiene (5 mmol) and acrolein (7.5 mmol) in diglyme (5 mL) was added the Lewis acid (0.25 mmol) and the mixture was stirred at room temperature for 60 min. [b] Determined by GC. [c] Under neat conditions for 40 min. [d] Reaction time 10 min with 89 % isolated yield of 3,4-dimethyl-3-cyclohexene-1-carbaldehyde. [e] Some by-products are visible by GC analysis.

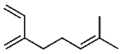
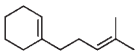
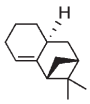
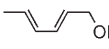
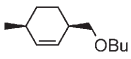
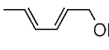
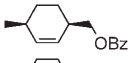
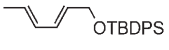
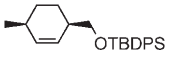
Again, it was necessary to quench the Lewis acid before the decarbonylation could be achieved. This could be performed by adding one equivalent of K_2HPO_4 relative to $BF_3 \cdot OEt_2$ together with a small amount of water which did not interfere with the ensuing decarbonylation reaction. On the contrary, neutralizing $BF_3 \cdot OEt_2$ with Na_2CO_3 or K_2CO_3

caused the decarbonylation to proceed slowly and gave rise to side products and precipitation of rhodium metal.

Earlier studies on simple aldehydes had shown that the decarbonylation could be achieved with an *in situ* generated catalyst from $RhCl_3 \cdot 3H_2O$ and dppp.[14] Addition of these two reagents to the Diels–Alder adduct did result in the desired decarbonylation upon heating, but the reaction was accompanied by severe double bond isomerization. It was not possible to add $RhCl_3 \cdot 3H_2O$ and dppp before the Diels–Alder reaction since dppp catalyzes a rapid polymerization of acrolein. Therefore, it was decided to use $[Rh(dppp)_2Cl]$ for the decarbonylation. This complex was prepared by a new one-step procedure where $RhCl_3 \cdot 3H_2O$ was treated with two equivalents of dppp in an ethanol solution at reflux for 30 min followed by removal of the solvent in vacuo. This afforded a crude $[Rh(dppp)_2Cl]$ complex which was equal in reactivity to the catalyst formed by the previous two-step procedure.[17] With 0.3% of the crude complex the decarbonylation could be achieved in 20 h to afford the desired 1,2-dimethylcyclohexene in 86% isolated yield from the starting diene (Table 2, entry 1). The progress of the decarbonylation could be monitored by measuring the evolution of carbon monoxide. Diglyme was removed in an aqueous work-up and the product was isolated by extraction with pentane and subsequent distillation.

Table 2. Acrolein as ethylene synthon in the Diels–Alder reaction.[a]



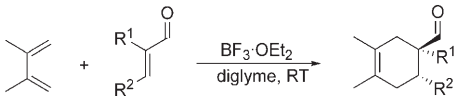
Entry	Diene	Product	Yield [%][b]
1			86
2			65
3			77
4			75
5			81
6			84
7[c]			79
8			66
9[d]			53
10[c]			61

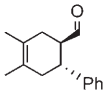
[a] Reactions were carried out on a 5–40 mmol scale in diglyme (1 M solution) with 6–10% of $BF_3 \cdot OEt_2$ for the Diels–Alder reaction (10–300 min at RT) and 0.3% of $[Rh(dppp)_2Cl]$ for the decarbonylation (8–20 h at reflux). [b] Isolated yield. [c] 1% $[Rh(dppp)_2Cl]$ was used. [d] Decarbonylation took 42 h.

To examine the scope and limitations of this new one-pot protocol, a number of other dienes were also subjected to the reaction with acrolein (Table 2, entries 2–10). In general, the Diels–Alder decarbonylation sequence worked very well for a variety of hydrocarbon dienes where yields around 80% were typically obtained (entries 2–6). It should be noted that some of the products are highly volatile and thus difficult to isolate quantitatively. Ether and ester functionalities can also be accommodated in the diene (entries 7–10), although the 1,4-disubstituted dienes in entries 8–10 reacted significantly slower than the other dienes. The longer reaction time in the Diels–Alder reaction resulted in a slightly decreased yield of the product cyclohexenes due to a slow acid-catalyzed decomposition of the allyl ether and ester dienes. No sign of a retro Diels–Alder reaction was observed when the intermediate aldehydes were heated to 162°C during the decarbonylation reaction. Several dienes failed to undergo the cycloaddition in the presence of $BF_3 \cdot OEt_2$. Furan underwent polymerization while dienes with conjugating electron-withdrawing groups such as sorbic aldehyde and β-ionone did not react with acrolein. In all cases, except for entry 1, did the Diels–Alder reaction furnish more than one aldehyde (regioisomers and *exo*/*endo* isomers). Particularly, the reaction with the 1,4-disubstituted dienes led to the formation of all four isomeric aldehydes. However, after decarbonylation they all gave rise to the same cyclohexene product which illustrates the benefit of the one-pot procedure where no work-up of the intermediate aldehyde is required.

Other α,β-unsaturated aldehydes as dienophiles: With the successful application of acrolein as an ethylene equivalent the studies were now extended to other unsaturated aldehydes. Since the Diels–Alder reaction is also highly sensitive to substituents in the dienophile it was decided first to examine the rate of the $BF_3 \cdot OEt_2$-catalyzed cycloaddition reaction with various aldehydes. As shown above, the reaction between 2,3-dimethyl-1,3-butadiene and acrolein goes to completion within 10 min in diglyme with 5% of $BF_3 \cdot OEt_2$ (Table 1, entry 4). Changing the solvent to diethyl ether had no influence on the rate of the cycloaddition (Table 3, entry 1). However, the reactions with substituted acroleins were slower and it was necessary to use a larger amount of the Lewis acid. With 10% of $BF_3 \cdot OEt_2$ the reaction with methacrolein went to completion in 30 min and proceeded very cleanly to give the product in high yield (entry 2). The reactions with crotonaldehyde and cinnamaldehyde were significantly more sluggish, but full conversion could still be obtained within a reasonable timeframe (Figure 1 and Table 3, entries 3 and 4). This, however, was not possible with 3-methylcrotonaldehyde where only trace amounts of the cycloaddition product was obtained even with very long reaction times and up to 30% of $BF_3 \cdot OEt_2$ (Figure 1). The use of other Lewis acids such as zinc chloride and bismuth triflate did not improve the yield of the cycloaddition product. In this connection, it should be noted that 3-methylcrotonaldehyde is known to give a poor yield in the thermal

Table 3. $BF_3{\cdot}OEt_2$-catalyzed Diels–Alder reaction with 2,3-dimethyl-1,3-butadiene and α,β-unsaturated aldehydes.[a]



Entry	Dienophile	$BF_3{\cdot}OEt_2$ loading [%]	Reaction time	Product	Yield [%][b]
1[c]		5	10 min		87
2		10	30 min		95
3		10	6 h		89
4		15	24 h		74

[a] Reactions were performed with 30 mmol of diene and 45 mmol of dienophile in 30 mL of diglyme. [b] Isolated yield. [c] Diethyl ether was used instead of diglyme.

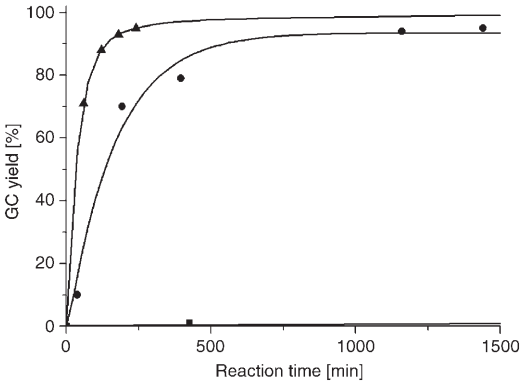
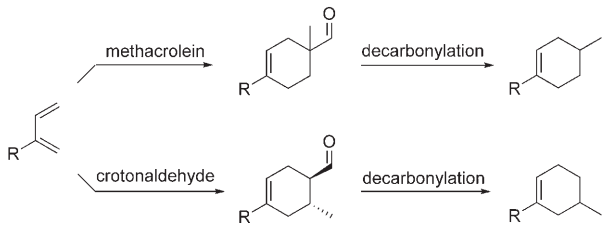


Figure 1. Comparison of the cycloaddition rate for crotonaldehyde (▲: 10% $BF_3{\cdot}OEt_2$), cinnamaldehyde (●: 15% $BF_3{\cdot}OEt_2$) and 3-methylcrotonaldehyde (■: 10% $BF_3{\cdot}OEt_2$) in the reaction with 2,3-dimethyl-1,3-butadiene.

Diels–Alder reaction[19] and we are not aware of any successful Lewis acid-catalyzed cycloadditions with this dienophile.

With the optimized cycloaddition reaction available the stage was now set to investigate the one-pot sequence with the substituted dienophiles. Methacrolein and crotonaldehyde can both serve as propylene equivalents, but will give rise to different regioisomeric products. Methacrolein will mainly afford the "*para*" product after decarbonylation while crotonaldehyde will furnish the corresponding "*meta*" product (Scheme 2). Unfortunately, the decarbonylation of the Diels–Alder adduct from methacrolein did not proceed at 162 °C. This is probably due to the steric bulk in the α-tribranched aldehyde (see Table 3, entry 2) and has previously been observed with a similar hindered aldehyde.[14] The temperature was therefore raised and it turned out that the neat tribranched aldehyde could be decarbonylated slowly at a temperature around 215 °C. However, under these forcing conditions the reaction was accompanied by small amounts of product from double-bond isomerization which could not be separated. As a result, it was decided to abandon methacrolein as a propylene synthon.

Instead, crotonaldehyde was examined and in this case the decarbonylation proceeded at 162 °C without any side reactions. Three different dienes were subjected to the one-pot Diels–Alder decarbonylation sequence in diglyme to afford the product cyclohexenes in good yields (Table 4, entries 1–3). In the latter two cases very small amounts of the corresponding regioisomers were also obtained according to analysis by GC-MS.



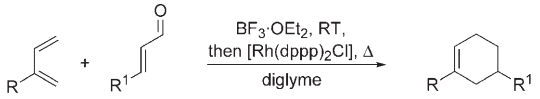
Scheme 2. Regioselectivity with methacrolein and crotonaldehyde.

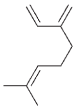
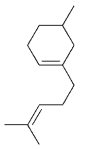
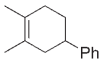
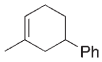
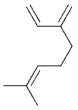
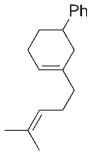
Cinnamaldehyde can serve as a styrene equivalent in the Diels–Alder reaction when followed by the decarbonylation. Although, the cycloaddition reaction with cinnamaldehyde is slower than for crotonaldehyde, the same three dienes still reacted to completion within 24 h (entries 4–6). Subsequent quenching of $BF_3{\cdot}OEt_2$ and heating with the rhodium catalyst achieved the decarbonylation in a satisfying overall yield and with excellent regioselectivity for the last two cases. It should be noted that this procedure with olefin equivalents gives rise to the opposite regioisomer as compared to the thermal Diels–Alder reaction with substituted olefins.[20] For example, the thermal reaction between isoprene and styrene at 200 °C affords the product in entry 5 as a 2:7 mixture of "*meta*" and "*para*" in 31% yield.[21]

Conclusion

In summary, we have shown that α,β-unsaturated aldehydes can serve as olefin equivalents in the $BF_3{\cdot}OEt_2$-catalyzed Diels–Alder reaction with 1,3-dienes when the cycloaddition

Table 4. Diels–Alder decarbonylation protocol with various α,β-unsaturated aldehydes.[a]



Entry	Diene	Dienophile	Major product	Regioisomer ratio	Yield [%][b]
1[c]				–	86
2[c]				24:1	67
3[c]				24:1	88
4[d]				–	73
5[d]				39:1	59
6[d]				39:1	75

[a] Reactions were carried out with 10–15% of $BF_3{\cdot}OEt_2$ for the Diels–Alder reaction and 0.3% of [Rh(dppp)$_2$Cl] for the decarbonylation (14–30 h). [b] Isolated yield of both isomers. [c] 10% of $BF_3{\cdot}OEt_2$ was used for 5–6 h. [d] 15% of $BF_3{\cdot}OEt_2$ was used for 24 h.

is combined with a rhodium-catalyzed decarbonylation in the same pot. In this way, the aldehyde group functions as a traceless control element which directs both reactivity and regioselectivity in the overall transformation. Acrolein, crotonaldehyde and cinnamaldehyde were shown to act as synthons for ethylene, propylene and styrene, respectively, and good yields were obtained of the product cyclohexenes. Although, the decarbonylation is performed at 162 °C, the reaction still tolerates a number of functional groups in the substrates including esters, silyl ethers and isolated olefins.[22] The two-step procedure generates only a minimum amount of waste compared to previous methods[7–11] since both reactions are performed with only a catalytic amount of an additive. Thus, we believe this procedure will be a valuable new tool for synthesis of certain cyclohexenes from cheap starting materials in an atom-economical fashion.

Experimental Section

General procedure for Diels–Alder decarbonylation sequence: A solution of $RhCl_3{\cdot}3H_2O$ (29.3 mg, 0.111 mmol) and dppp (95.6 mg, 0.225 mmol) in ethanol (10 mL) was degassed and heated to reflux for 30 min. The mixture was then concentrated to afford crude [Rh(dppp)$_2$Cl] as a yellow solid which was dissolved in diglyme (2 mL). Another flask was charged with diglyme (40 mL), diene (39 mmol) and aldehyde (60 mmol) followed by addition of $BF_3{\cdot}OEt_2$ (0.30–0.74 mL, 2.4–5.9 mmol). The mixture was stirred at room temperature until the cycloaddition had gone to completion according to GC or TLC. The mixture was quenched with $K_2HPO_4{\cdot}3H_2O$ (0.60–1.2 g, 2.4–5.9 mmol) and water (0.25 mL). The above catalyst solution was added and the reaction was degassed and heated to reflux until the decarbonylation had gone to completion. The mixture was cooled to room temperature, diluted with water (50 mL) and extracted with pentane (5×50 mL). The combined organic phases were washed with water (5×50 mL) and dried with anhydrous Na_2SO_4. Pentane was removed by distillation followed by isolation of the product cyclohexene by either distillation or flash chromatography. The decarbonylation could be monitored by measuring the evolution of carbon monoxide. This was achieved by connecting the reaction flask to a burette filled with water. The bottom of the burette was further connected to a reservoir flask with water. In this way, carbon monoxide from the reaction forces water from the burette into the reservoir flask.

1,2-Dimethylcyclohexene: b.p. 134–136 °C (lit.[11] b.p. 135–136 °C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.50–1.60 (m, 4H), 1.61 (s, 6H), 1.86–1.97 ppm (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.14, 23.46, 31.71, 125.60 ppm; MS: m/z: 110 $[M]^+$.

1-Methylcyclohexene: b.p. 107–110 °C (lit.[23] b.p. 106–110 °C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.49–1.67 (m, 4H), 1.64 (s, 3H), 1.87–2.01 (m, 4H), 5.36–5.42 ppm (tdd, 1H, J = 1.5, 3.4, 5.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.37, 22.99, 23.94, 25.28, 30.02, 121.10, 134.05 ppm; MS: m/z: 96 $[M]^+$.

1-(4-Methyl-3-pentenyl)cyclohexene: b.p. 100–102 °C at 17 mm Hg; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.48–1.66 (m, 4H), 1.60 (s, 3H), 1.68 (s, 3H), 1.88–2.12 (m, 8H), 5.06–5.15 (m, 1H), 5.37–5.42 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 17.65, 22.57, 23.02, 25.23, 25.69, 26.46, 28.37, 38.09, 120.66, 124.47, 131.23, 137.72 ppm; MS: m/z: 164 $[M]^+$. NMR data are in accordance with literature values.[7b]

Bicyclo[2.2.2]-2-octene: ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.10–1.19 (m, 4H), 1.36–1.46 (m, 4H), 2.35–2.43 (m, 2H), 6.12–6.19 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.75, 29.46, 134.21 ppm; MS: m/z: 108 $[M]^+$. NMR data are in accordance with literature data.[7b]

9,9-Dimethyltricyclo[4,4,0,1^{8,10}]-1-undecene: b.p. 115–120 °C at 15 mm Hg (lit.[7b] b.p. 118–123 °C at 15 mm Hg); $[\alpha]_D^{20}$ = −29.9 (c = 2.2, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.84 (d, 1H, J = 9.3 Hz), 0.97 (s, 3H), 1.13–1.23 (m, 1H), 1.25 (s, 3H), 1.40–1.48 (m, 1H), 1.56–1.71 (m, 1H), 1.76–1.90 (m, 2H), 1.94–2.11 (m, 3H), 2.11–2.24 (m, 1H), 2.41 (t, 1H, J = 5.8 Hz), 2.45–2.61 (m, 2H), 5.14 ppm (q, 1H, J = 3.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.79, 23.57, 24.53, 27.19, 32.56, 33.37, 33.55, 35.59, 39.56, 42.17, 52.22, 116.88, 146.73 ppm; MS: m/z: 176 $[M]^+$.

1-Phenylcyclohexene: b.p. 122–125 °C at 13 mm Hg (lit.[24] b.p. 128 °C at 16 mm Hg); R_f = 0.45 (EtOAc/hexane 1:99); ^{1}H NMR ($CDCl_3$, 300 MHz):

δ = 1.63–1.73 (m, 2H), 1.75–1.84 (m, 2H), 2.18–2.27 (m, 2H), 2.39–2.47 (m, 2H), 5.13–5.19 (m, 1H), 7.19–7.42 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.40, 23.31, 26.12, 27.63, 125.00, 125.16, 126.73, 128.40, 136.80, 142.92 ppm; MS: *m*/*z*: 130 $[M-C_2H_4]^+$.

1-(Butoxymethyl)cyclohexene: b.p. 95–102 °C at 15 mm Hg; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.90 (t, 3H, *J* = 7.3 Hz), 1.30–1.43 (m, 2H), 1.49–1.68 (m, 6H), 1.93–2.05 (m, 4H), 3.35 (t, 2H, *J* = 6.6 Hz), 3.78–3.80 (m, 2H), 5.63–5.69 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.92, 19.39, 22.42, 22.52, 24.97, 25.86, 31.85, 69.62, 75.56, 124.47, 135.21 ppm; HRMS: *m*/*z*: calcd for $C_{11}H_{20}ONa$: 191.1412 $[M+Na]^+$; found: 191.1403.

3-(Butoxymethyl)-6-methylcyclohexene: R_f = 0.67 (Et_2O/pentane 1:19); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.87–0.97 (m, 6H), 1.21–1.45 (m, 3H), 1.48–1.72 (m, 5H), 2.09–2.39 (m, 2H), 3.19–3.31 (m, 2H), 3.36–3.46 (m, 2H), 5.52–5.66 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.94, 19.37, 21.43, 23.15, 27.95, 29.99, 31.81, 35.26, 70.81, 74.56, 127.25, 134.88 ppm; HRMS: *m*/*z*: calcd for $C_{12}H_{22}ONa$: 205.1568 $[M+Na]^+$; found: 205.1563.

(4-Methyl-2-cyclohexenyl)methyl benzoate: R_f = 0.55 (EtOAc/heptane 1:99); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.00 (d, 3H, *J* = 7.1 Hz), 1.30–1.45 (m, 1H), 1.56–1.79 (m, 3H), 2.15–2.27 (m, 1H), 2.50–2.61 (m, 1H), 4.20 (d, 1H, *J* = 1.3 Hz), 4.22 (s, 1H), 5.58–5.76 (m, 2H), 7.40–7.59 (m, 3H), 8.03–8.08 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.27, 23.03, 27.73, 29.82, 34.42, 67.90, 125.81, 128.29, 129.51, 130.36, 132.81, 135.95, 166.56 ppm; HRMS: *m*/*z*: calcd for $C_{15}H_{18}O_2Na$: 253.1205 $[M+Na]^+$; found: 253.1206.

***tert*-Butyl((4-methyl-2-cyclohexenyl)methoxy)diphenylsilane**: R_f = 0.30 (EtOAc/heptane 1:39); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.99 (d, 3H, *J* = 3.7 Hz), 1.11 (s, 9H), 1.22–1.34 (m, 1H), 1.63–1.75 (m, 3H), 2.13–2.42 (m, 2H), 3.50–3.65 (m, 2H), 5.57–5.70 (m, 2H), 7.37–7.49 (m, 6H), 7.70–7.76 ppm (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.30, 21.39, 22.72, 26.87, 27.97, 29.99, 37.74, 67.32, 127.28, 127.56, 129.48, 133.98, 134.89, 135.60; HRMS: *m*/*z*: calcd for $C_{24}H_{32}OSiNa$: 387.2120 $[M+Na]^+$; found: 387.2120.

1,2,4-Trimethylcyclohexene: b.p. 150–154 °C (lit.[25] b.p. 154 °C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.94 (d, 3H, *J* = 2.6 Hz), 1.08–1.23 (m, 1H), 1.24–1.70 (m, 9H), 1.85–2.11 ppm (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 18.86, 19.10, 21.95, 29.32, 31.73, 31.98, 40.53, 125.14, 125.16 ppm; MS: *m*/*z*: 124 $[M]^+$.

1,5-Dimethylcyclohexene: b.p. 132–133 °C (lit.[26] b.p. 127–129 °C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.93–0.98 (m, 3H), 1.03–1.19 (m, 1H), 1.51–1.73 (m, 6H), 1.87–2.06 (m, 3H), 5.33–5.40 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.97, 23.74, 25.36, 28.89, 30.63, 38.73, 120.64, 133.65 ppm; MS: *m*/*z*: 110 $[M]^+$.

5-Methyl-1-(4-methyl-3-pentenyl)cyclohexene: b.p. 107–108 °C at 12 mm Hg; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.96 (d, 3H, *J* = 2.7 Hz), 1.05–1.22 (m, 1H), 1.54–1.75 (m, 9H), 1.87–2.13 (m, 7H), 5.06–5.16 (m, 1H), 5.35–5.41 ppm (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 17.67, 22.00, 25.33, 25.70, 26.49, 28.92, 30.83, 37.07, 37.91, 120.26, 124.47, 131.22, 137.29 ppm; MS: *m*/*z*: 178 $[M]^+$.

1,2-Dimethyl-4-phenylcyclohexene: b.p. 130–131 °C at 13 mm Hg (lit.[27] b.p. 128–130 °C at 11 mm Hg); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.65–1.70 (m, 6H), 1.71–2.29 (m, 6H), 2.73–2.86 (m, 1H), 7.18–7.38 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 18.87, 19.05, 30.29, 32.35, 40.05, 40.91, 125.32, 125.48, 125.85, 126.84, 128.28, 147.32 ppm; MS: *m*/*z*: 186 $[M]^+$.

1-Methyl-5-phenylcyclohexene: b.p. 122–123 °C at 13 mm Hg; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.58–1.74 (m, 1H), 1.68 (s, 3H), 1.83–1.93 (m, 1H), 2.01–2.20 (m, 4H), 2.78–2.90 (m, 1H), 5.42–5.49 (br s, 1H), 7.14–7.33 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 23.62, 25.82, 29.45, 38.31, 40.54, 120.86, 125.91, 126.86, 128.32, 133.77, 147.30 ppm; MS: *m*/*z*: 172 $[M]^+$. ^{13}C NMR data are in accordance with literature data.[28]

5-Phenyl-1-(4-methyl-3-pentenyl)cyclohexene: b.p. 113–115 °C at 0.1 mm Hg; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.65 (s, 3H), 1.74 (s, 3H), 1.67–1.80 (m, 1H), 1.90–2.27 (m, 9H), 2.76–2.90 (m, 1H), 5.13–5.21 (m, 1H), 5.53 (br s, 1H), 7.20–7.39 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 17.70, 25.71, 25.83, 26.45, 29.61, 36.81, 37.79, 40.59, 120.47, 124.30, 125.91, 126.86, 128.32, 131.38, 137.45, 147.37 ppm; MS: *m*/*z*: 240 $[M]^+$; elemental analysis (%) calcd for $C_{18}H_{24}$: C 89.94, H 10.06; found: C 89.58, H 10.12.

Acknowledgement

Financial support from the Lundbeck Foundation is gratefully acknowledged. The Center for Sustainable Green Chemistry is funded by the Danish National Research Foundation.

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Received: January 2, 2008
Published online: May 9, 2008

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Gold nanoparticle catalyzed oxidation of alcohols

From biomass to commodity chemicals

ABSTRACT

One of the greatest challenges that the chemical industry faces today is to become less dependent on fossil resources, and oil in particular. One way of addressing this challenge is to find ways to transform renewable resources into commodity chemicals. Renewable resources such as carbohydrates and glycerol are rich in alcohol functionalities. Thus, a key step in utilizing these resources lies in the conversion of this functional group.
Benign oxidations involving oxygen as the stoichiometric oxidant are important from both an environmental and economical perspective.
Recently, it has become clear that supported gold nanoparticles are highly active catalysts for oxidizing alcohols and aldehydes using oxygen as the oxidant. This perspective will focus on the use of gold nanoparticles in the oxidation of renewables.

INTRODUCTION

Gold has always been able to fascinate man and it plays a central role in our society. The alchemical dream of turning lead into gold has laid the foundation for the modern field of chemistry. Although gold has in a way acted as a catalyst in this regard, gold as an element has unofficially been declared catalytically inactive for a long time. In recent years, however, the field of gold catalysis has emerged to become one of fastest growing fields in catalysis at the moment (1).
This modern gold rush was sparked by several events. In 1973, Bond et al. reported that olefins can be hydrogenated over supported gold catalysts (2). Some 12 years later, in 1985, Hutchings calculated and demonstrated that gold is the most active metal catalyst for the hydrochlorination of acetylene (3). Simultaneously, Haruta demonstrated that gold, when dispersed as nanoparticles, can oxidize CO at temperatures as low as –72°C (4).
The breakthrough in the area of alcohol oxidation came in 1998 when Prati and Rossi reported that supported gold nanoparticles can facilitate the oxidation of diols with oxygen, and that gold can be more selective than platinum and palladium for this reaction (5). This event sparked further focus on the use of gold nanoparticles as an oxidation catalyst for alcohols (6-7). Gold nanoparticles have also been used in the oxidation of propylene to form propylene oxide (8) and it has been demonstrated that even unfunctionalized compounds such as cyclohexane can be oxidized to cyclohexanol and cyclohexanone over a gold catalyst (9). More recently, Hutchings have demonstrated that hydrogen can be oxidized to hydrogen peroxide by the use of bimetallic gold nanoparticles, thereby opening up for the possibility of producing hydrogen peroxide *in situ*, and avoiding the handling of hazardous hydrogen peroxide solutions (10).
The use of gold as a catalyst could seem problematic in economic terms due to the high cost of gold. However, compared to palladium and platinum, which are both widely used as catalysts throughout the field of chemistry, gold is similarly priced (figure 1). Therefore, the use of gold should not be precluded from an economical perspective. However, the gold catalysts are required to be highly active, selective and reusable in order for them to be economically attractive alternatives.

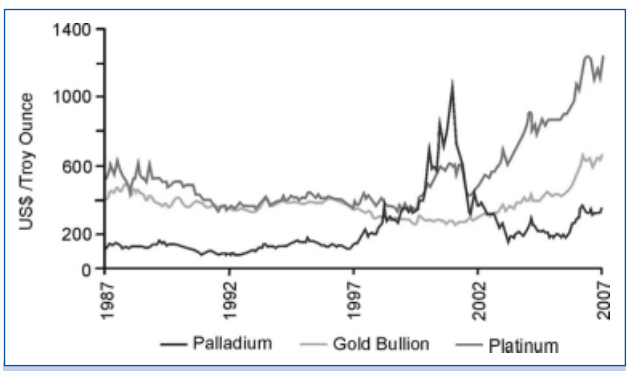


Figure 1. Graph of gold, palladium and platinum prices for the past 20 years.

GOLD NANOPARTICLES

Various methods exist for the preparation of the gold nanoparticles, such as deposition-precipitation, co-precipitation and impregnation. Each method results in a different size distribution of the gold nanoparticles, which can be determined by *e.g.* TEM measurements (Figure 2). Gold nanoparticles are by definition particles smaller than 100 nm in size. However, only very small nanoparticles (<10 nm) are highly active for the oxidation of alcohols (11). In an interesting study by Rossi and co-workers, it is demonstrated that unsupported gold nanoparticles are able to catalyze the oxidation of glucose to gluconic acid (12). In this case, the gold nanoparticles are only active for a few minutes, due to the sintering of the gold particles, resulting in the formation of larger, inactive gold nanoparticles, thus illustrating

the importance of the support. The support however, plays a more important role than merely acting as surface for gold nanoparticles to avoid sintering. In one important study by Corma and co-workers, nanocrystalline ceria is reported to be a highly active support for the oxidation of simple alkyl and aryl alcohols (6). The nanocrystalline ceria is in this case capable of oxidizing alcohols and is then re-oxidized with oxygen by the gold nanoparticles. In other cases, such as the oxidation of polyols, carbon supports are found to be more active than ceria, illustrating that gold nanoparticle catalyzed oxidation can be fine tuned by the use of different supports (13). Many reports on gold catalyzed alcohol oxidation also point to the finding that base such as sodium hydroxide acts as a promoter for the gold catalyst, this is particularly the case if the product formed is a carboxylic acid which lowers the pH-value of the solution (14).

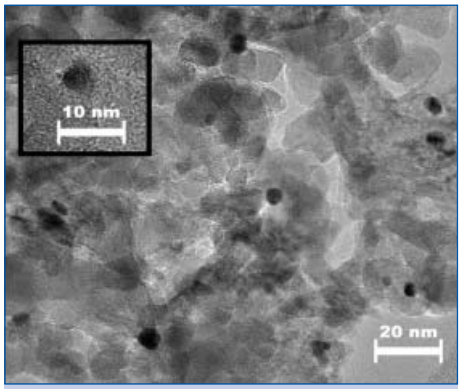


Figure 2. TEM image of 1 wt% Au on spinel.

However, it has also been demonstrated that alcohols can be oxidized to carboxylic acids at more forcing conditions without the use of a base promoter (15). Depending on the reaction conditions, primary alcohols can be oxidized into aldehydes, carboxylic acids or esters (Scheme 1). When a primary alcohol is oxidized without the use of a solvent, the major product is the corresponding aldehyde. When water is present, the major product becomes the carboxylic acid, presumable formed from oxidation of the aldehyde hydrate (6). If methanol is used as solvent instead, methyl esters are formed in high selectivity. This is explained analogously by oxidation of the intermediate aldehyde hemiacetal, thereby directly furnishing the methyl ester (16). Methanol is oxidized much slower than a primary alcohol, so only small amounts of methanol oxidation takes place during this oxidative esterification reaction.

OXIDATION OF ETHANOL

Acetic acid is a highly important industrial chemical and ranks among the 50 largest chemicals by volume produced globally (17). Currently, acetic acid is produced mainly by carbonylation of methanol, and thus it originates exclusively from fossil resources. As the price of fossil resources, such as oil and natural gas, steadily increases, other feedstocks become interesting as a basis for chemical production. Ethanol is one such feedstock and it can be considered a renewable resource since it is readily formed by fermentation of carbohydrates and is already available in vast amounts. One of the simplest uses of ethanol is as a feedstock for the production of acetic acid.

Biologically, acetic acid can also be formed directly by fermentation. However, for practical reasons this process has limitations, mainly due to the fact that the bacteria do not thrive under the acidic conditions in the resulting reaction mixture. One alternative to the biological route is to oxidize ethanol to acetic acid over a heterogeneous catalyst (15). By employing gold nanoparticles supported on spinel ($MgAl_2O_4$), a 5 wt% aqueous ethanol solution can be oxidized to acetic acid in above 90 percent yield by the use of oxygen as the only stoichiometric reagent. Interestingly, gold nanoparticles are much more selective than palladium and platinum, which both cause significant over-oxidation, resulting in the formation of CO_2.

The same procedure can be used for production of ethyl acetate by simply increasing the ethanol concentration. Thus, a 75 wt% aqueous ethanol solution was oxidized to ethyl acetate with 50 percent selectivity at 85 percent conversion (18).

This change in selectivity is explained by the competition between water and ethanol in the formation of either the acetaldehyde hydrate or the acetaldehyde hemiacetal, resulting in the formation of acetic acid and ethyl acetate, respectively.

OXIDATION OF GLYCEROL

Currently, glycerol is considered a waste product from the production of biodiesel. For every tonne of biodiesel produced, about 100 kg glycerol is also formed. Alternatively, glycerol can be produced simply by fermentation of glucose under proper conditions. Glycerol is a highly functionalized molecule, which has proven difficult to selectively convert into useful chemicals. However, gold catalysis could prove to be an important tool in the valorisation of glycerol (19). In 2002, Hutchings and co-workers demonstrated that glycerol in the presence of aqueous base can be oxidized with 100 percent selectivity at 56 percent conversion into glyceric acid over carbon supported gold nanoparticles (14). In comparison, palladium and platinum catalysts results in the formation of dihydroxyacetone as the major product (20). The oxidation of glycerol has been examined extensively and is one of the most studied areas within the field of gold catalyzed oxidations recently (11, 13-14, 19, 21-23). Various supports have been examined, and carbon supported catalysts are found to be more active than metal oxide

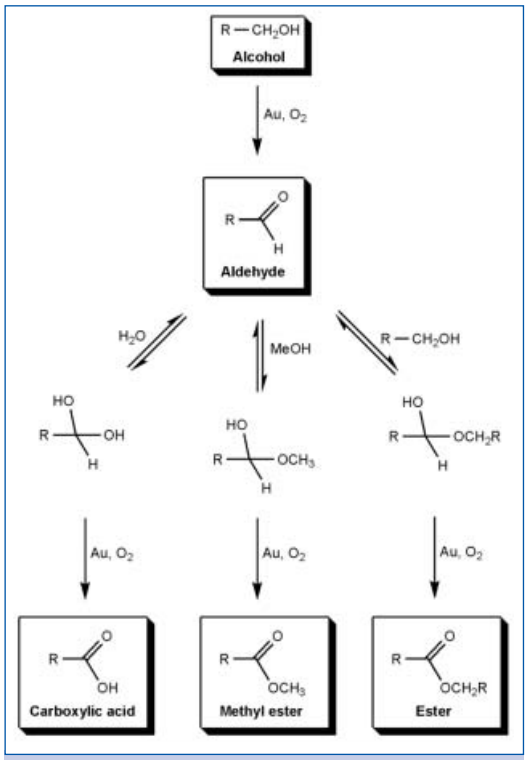
supported catalysts for glycerol oxidation (5, 13, 22). The size of the gold nanoparticles is also a very important reactivity parameter. Small gold nanoparticles (5 nm) are most active, whereas larger gold nanoparticles (20 nm) are more selective towards glyceric acid (11). When oxidizing glycerol in water, high pH-values are necessary in order for the oxidation to take place. In fact, no reaction takes place in the absence of base (14). As the glyceric acid formed will neutralize one equivalent of base, a stoichiometric amount of base is required for oxidizing glycerol into glyceric acid.

An alternative approach to the aqueous oxidation is to conduct the oxidation in methanol. These oxidative esterification conditions will result in the formation of methyl glycerate rather than glyceric acid. This product does not lower the pH-value of the reaction mixture, and a catalytic amount of base is thus capable of promoting the oxidation. Furthermore, the methyl glycerate formed can undergo further oxidation to form dimethyl tartronate and dimethyl mesoxalate with 89 percent selectivity at full conversion, by the use of a gold on titania or gold on iron oxide (24). The added benefit of this approach is that the glycerol waste stream from biodiesel production contains a mixture of glycerol, methanol and base. This approach could therefore, in principle, utilize the waste stream for chemical production.

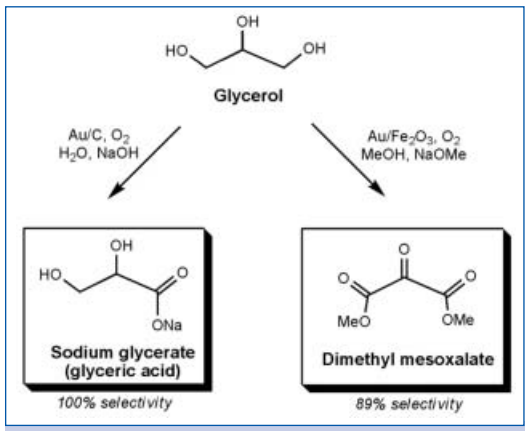
Currently, these products find limited use. However, when available in large amounts through inexpensive routes, glyceric acid and sodium glycerate could be interesting as e.g. pH-buffers in the food industry.

Oxidation of propanediols

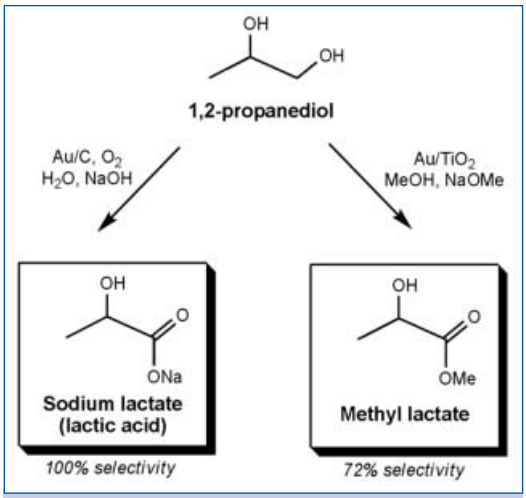
Another possibility of valorising glycerol is by hydrogenation to 1,2-propanediol and 1,3-propanediol. Gold catalyzed oxidation of aqueous 1,2-propanediol have been reported to result in the formation of lactic acid with 100 percent selectivity at 30 percent conversion (5). Lactic acid is an attractive product, since it can be used for the production of biodegradable polymers. It is currently produced via fermentation of glucose, and a cheap process employing a heterogeneous catalyst would be an interesting improvement in this area.



Scheme 1. Gold catalyzed oxidation of alcohols can lead to various products, depending on the reaction conditions.



Scheme 2. Oxidation of glycerol to furnish sodium glycerate (13) and dimethyl mesoxalate (22).



Scheme 3. Oxidation of 1,2-propanediol to form sodium lactate (5) and methyl lactate (22).

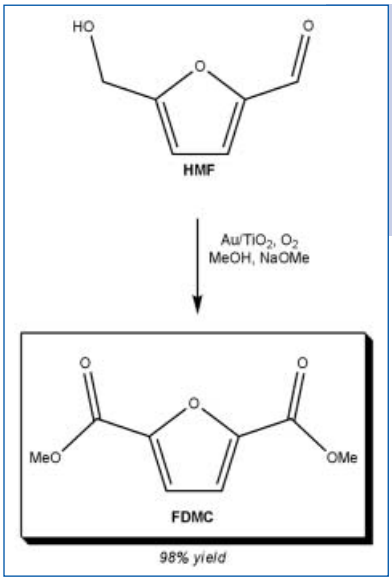
Oxidation of 1,2-propanediol and 1,3-propanediol in methanol over a titania supported gold catalyst have also been reported (16, 24). 1,2-propanediol is oxidized to methyl lactate in 72 percent selectivity at full conversion (scheme 3). 1,3-propanediol is oxidized to methyl 3-hydroxypropionate in 90 percent selectivity at 94 percent conversion. The latter can be dehydrated to furnish methyl acrylate, another important polymer building block in the chemical industry. In contrast to metal oxide catalyzed oxidative dehydrogenation of glycerol where acrylic acid is formed, this approach offers direct formation of methyl acrylate (25).

OXIDATION OF CARBOHYDRATES

Carbohydrates are the most abundant class of biomass. Cheap and efficient ways of converting this resource into useful chemicals are therefore of central importance if the chemical industry has to become less dependant on fossil resources. Currently, most of the processes that utilize glucose as feedstock involve biochemical processes. One example of this is the biochemical oxidation of glucose to gluconic acid, a 60.000 tonne per year process. Recently, oxidation of glucose to gluconic acid was achieved with 100 percent selectivity at very mild conditions (26-27). Interestingly, the alumina supported gold catalyst was demonstrated to be very durable for this reaction, with no loss of catalytic activity after 20 batch runs (27).

The use of a heterogeneous gold catalyst in place of enzymes enables facile recycling of the catalyst by filtration. Furthermore, different pH-range can be utilized in the process, as well as higher temperatures are tolerated by the gold catalyst (28).

Another approach in the utilization of carbohydrates for the production of chemicals is by dehydration. Dehydration is typically achieved with a simple acidic catalyst such as HCl in DMSO and is an elegant way to remove functionality from the carbohydrate without the use of any reagents (29). Pentoses are dehydrated to furfural, while hexoses such as glucose and fructose are converted to hydroxymethyl furfural (HMF). Both chemicals are thus available directly from biomass and are



Scheme 4. Oxidation of HMF to form FDMC, a potential polymer building block can be achieved by the use of a gold catalyst and air (26).

therefore interesting starting materials for the production of chemicals. Recently, gold catalyzed oxidation of furfural and HMF in methanol was described (30). In this work, HMF was oxidized to furan-2,5-dimethylcarboxylate (FDMC) in 98 percent yield by the use of a gold on titania catalyst (scheme 4). FDMC is an interesting bi-functionalized compound, which has been proposed as a possible replacement for tere-phthalic acid used to produce soda bottles.

Thus, a new generation of chemical compounds and materials is emerging from biomass and will be able to substitute existing materials or be used for entirely new purposes. The need for new transformation reactions that are catalytic, highly efficient and economic is greater than ever, therefore gold catalysis will undoubtedly receive increasing focus in the coming years.

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Catalysis Letters, Vol. 116, Nos. 1–2, July 2007 (© 2007)
DOI: 10.1007/s10562-007-9086-9

Direct aerobic oxidation of primary alcohols to methyl esters catalyzed by a heterogeneous gold catalyst

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Received 10 March 2007; accepted 13 March 2007

Methyl esters can be produced in high yields by oxiding methanolic solutions of primary alcohols with dioxygen over a heterogeneous gold catalyst. The versatility of this new methodology is demonstrated by the fact that alkylic, benzylic and allylic alcohols, as well as alcohols containing an amine functionality are oxidized in good to excellent yields.

KEY WORDS: gold catalysis; catalytic oxidations; air; ester synthesis; methyl esters.

1. Introduction

One of the cornerstones of organic chemistry is the oxidation of alcohols to yield aldehydes, ketones, carboxylic acids and carboxylic acid derivatives. Today, these oxidations are most often carried out by the use of either stoichiometric amounts of heavy metal oxidants containing, e.g. chromium or manganese, or very expensive oxidants such as the Dess-Martin periodinane. Recently, more green approaches employing the ultimate oxidation agent, namely O_2, have been exploited [1–4].

Many methyl esters are industrially important chemicals, both as products in e.g. the perfume industry as solvents, extractants, diluents and as intermediates. An environmentally friendly route to such chemicals would be an important step towards a more green chemical industry. Here, we report that a range of primary alcohols in methanol can be selectively oxidized by dioxygen to the corresponding methyl esters using Au/TiO_2 as outlined in figure 1.

For the past two decades, the use of gold catalysts to facilitate simple aerobic oxidations has received considerable attention [5–8]. The field was pioneered by Haruta and co-workers who showed that CO can be oxidized into CO_2 by O_2 using Au/Fe_2O_3 [9, 10] and by Hutchings and co-workers who showed that acetylene can be hydrochlorinated using gold catalysts [11]. In recent years, the field has gained momentum following the observation that both aldehydes, ketones and carboxylic acids can be prepared by gold-mediated aerobic oxidations [12–17]. Currently, there is considerable interest in establishing a mechanistic understanding of the oxidations over heterogeneous gold catalysts. It is clear that special sites that only exist on gold nanoparticles are decisive for the unique catalytic activity [18, 19].

So far, the oxidation of carbon monoxide into carbon dioxide has most attracted interest in the rapidly growing area of heterogeneous gold catalysis. However, it has also become increasingly clear that the aerobic oxidation of various organic compounds, in particular compounds with C–O groups could provide "green" routes to a range of commodity chemicals and specialty chemicals. Obviously, selective oxidation with dioxygen is preferable to using any other oxidating agent, since oxygen is readily available and in ideal cases, the only byproduct is water. However, typically it has been a challenge to suppress the complete oxidation reaction that leads to the undesired formation of carbon dioxide. Recently, we showed that gold catalyst were efficient in oxidizing aqueous solutions of ethanol into acetic acid in high yields. This provides an alternative route to produce the key commodity chemical acetic acid by a sustainable and green approach in the sense that the feedstock is derived solely from renewable and no harmful byproducts are formed [17]. It has previously been shown by Hutchings and co-workers that oxidation of neat primary alcohols can lead to selective formation of the aldehydes [16]. Thus, it is clear that the solvent plays a significant role in the aerobic oxidation of primary alcohols. To further expand the range of products that are available by selective aerobic oxidation of alcohols with gold catalysts, we decided to explore the direct synthesis of esters by conducting the oxidation using methanol as the solvent. Methanol was chosen, since this would lead to formation of

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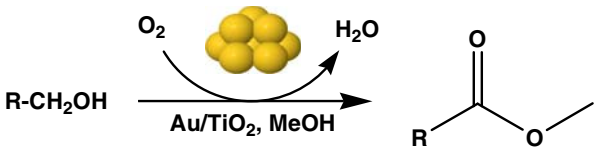

Figure 1. Schematic illustration of the selective aerobic oxidation of primary alcohols into esters using heterogeneous gold catalysts.

methyl esters that in many cases are important products or intermediates. Additionally, it appears that small primary alcohols are significantly more difficult to oxidize than larger, more substituted primary alcohols and this is obviously a prerequiste for achieving selective oxidations.

The oxidation of primary alcohols to carboxylic acids can be envisaged to proceed via an aldehyde intermediate followed by formation of the hydrate, which is subsequently oxidized to the carboxylic acid. A common by-product from the oxidation of primary alcohols is the corresponding ester. Indeed, in the absence of water, Corma and co-workers reported that the main product from oxidation of 3-phenyl-1-propanol was 3-phenylpropyl-3-phenylpropionate (in 88% yield) [15]. This can be easily explained since formation of the aldehyde hydrate is not possible, and the aldehyde will then form a hemiacetal with the alcohol. This hemiacetal can be further oxidized in the same manner as the aldehyde hydrate, leading to the corresponding ester as shown in figure 2.

The direct formation of methyl esters from the oxidation of primary alcohols in methanol is well known [20–24]. However, these methods all employ stoichiometric oxidants such as iodine [20], trichloroisocyanuric acid [21], (diacetoxy)iodobenzene [22] or hypochlorite reagents [23, 24]. The use of air as the oxidant in this transformation is still in its infancy. So far, only the oxidation of ethylene glycol to methyl glycolate has been described [25], and yet plans are already underway for industrializing the process [8].

The existing methodologies suggest that primary alcohols are oxidized more readily than methanol. Therefore, we decided to examine if primary alcohols can more generally be selectively oxidized to methyl esters by carrying out a gold catalyzed aerobic oxidation in methanol.

2. Experimental

2.1. Materials and equipment used

The supported gold catalyst used in this study, 1 wt% Au/TiO_2, was acquired from the World Gold Council (Gold reference catalyst #02-06, Sued-Chemie Catalysts Japan).

All chemicals were purchased from commercial sources and used without further purification: Methanol (99.9% pure, Sigma-Aldrich), 1-hexanol (98%, Riedel-de Haën), sodium methoxide solution (30 wt% in methanol, Sigma-Aldrich), cinnamyl alcohol (98%, Sigma-Aldrich), benzyl alcohol (>99%, Bie & Berntsen), 2-(hydroxymethyl) pyridine (98%, Aldrich), 1-adamantane methanol (99%, Aldrich) and dioxygen (>99.6%, Strandmøllen).

The autoclave used was a 325 mL titanium stabilized T316 autoclave, from the Parr Instrument Company.

The GC used for analyzing liquid reaction mixtures was an Agilent Technologies 6890N Network GC System equipped with a flame ionization detector (FID) and a DB-1 column (50 m × 0.320 mm, 5.00 micron, J&W Scientific, catalog 1231055). The GC program used was: 200 °C, hold 3 min; 250 °C, rate 20 °C/min, hold 20 min.

The GC used for analyzing gas mixtures was a Shimadzu GC-17A equipped with a thermal conductivity detector (TCD).

All NMR-spectra were recorded on a Varian Mercury 300 MHz instrument. Chemical shifts were correlated relative to chloroform. The data were processed with MestReC 4.7.4.0 software.

Transmission electron microscopy (TEM) was performed on a JEM 2000FX with an accelerating voltage of 300 kV. A few mg of the powdered samples was suspended in 2 mL ethanol, and the suspension was sonicated for 1 h. Then, the suspension was allowed to settle for 15 min, before a drop was taken and dispersed on a 300 mesh copper grid coated with holey carbon film.

2.2. Catalytic experiments

The autoclave was charged with Au/TiO_2 catalyst, methanol, substrate, and in some cases an additive

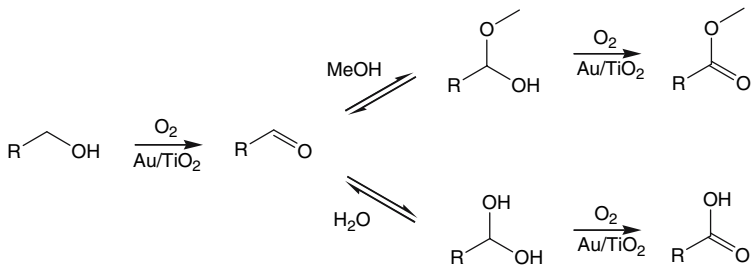

Figure 2. Proposed reaction pathway for the formation of methyl esters in methanol and carboxylic acids in water during aerobic oxidation of primary alcohols with heterogeneous gold catalysts.

(either 30 wt% sodium methoxide in methanol or 37 wt% hydrochloric acid in water) was added with a pipette, see table 1 for specific details. A 3 cm magnetic stir bar was fitted in the autoclave which was then pressurized with dioxygen. The autoclave was placed in a 130 °C preheated oil bath, and the reaction mixture was stirred rapidly. The autoclave was removed from the oil bath after the specified reaction time and was allowed to cool to room temperature.

2.3. Analysis of reaction mixtures

Ca. 1 mL of the reaction mixture was transferred to a centrifuge vial and centrifuged. The clear liquid was analyzed by GC by injecting 0.2 μL into the GC. Retention times of the products were verified by comparison to authentic reference samples. Conversion and selectivity were calculated with respect to the substrate.

In order to determine the extent of methanol oxidation, a plastic balloon with a vent was flushed three times with dinitrogen and evacuated. The balloon was then filled with gas from the autoclave, and the gas was analyzed using GC and referenced to a gas sample containing 2 mol% CO_2.

2.4. Isolation of products

In order to verify the results of the GC analyses we isolated the reaction products after some of the experiments using standard procedures and confirmed their purity by ^{1}H NMR. Methyl hexanoate (table 1, Entry 11) and methyl benzoate (table 1, Entry 13) were isolated by extraction with pentane and subsequently purified by Kugel-rohr distillation. However, in order to isolate methyl cinnamate (table 1, Entry 14) it was necessary to remove the methyl benzoate byproduct by flash chromatography after the initial pentane extraction using a small amount of heptane as solvent (3 cm in diameter column; eluent: heptane:ethyl acetate 19:1; rf: 0.2). Methyl pyridine-2-carboxylate was isolated by distillation.

3. Results and discussion

To determine the size of the gold particles we recorded about 40 high-resolution TEM images of the 1 wt% Au/TiO_2 catalyst used in this study. Based on this TEM study, the gold nanoparticles have a quite narrow size distribution with more than 95% of the gold particles having a diameter of 2–5 nm. A representative TEM image of the Au/TiO_2 catalyst is shown in figure 3.

Initially, the effect of pH on the reaction was studied by addition of either acid (HCl) or base ($NaOCH_3$) to the reaction mixture, see figure 4. As seen in figure 4, the additive plays an important role, both in terms of conversion of 1-hexanol and in terms of selectivity towards methyl hexanoate. Under acidic conditions, conversion of 1-hexanol is very low, and the major product is the dimethyl acetal of hexanol. This result suggests that the hemiacetal intermediate is converted to the acetal under acidic conditions, and that this compound is relatively inert to further oxidation. Under neutral and basic conditions, conversion of hexanol is much higher, and methyl hexanoate is formed with a much better selectivity. However, conversion and selectivity increases only slightly when going from neutral to more basic conditions. This observation is in contrast to the oxidation of diols and glycerol to carboxylic acids, where the presence of base is essential to the oxidation reaction [12, 14], since it clearly shows that methyl hexanoate can

Table 1
Experimental details[a]

Entry	MeOH V (mL)	Substrate	Molar ratio[b]	V (mL)	Additive	Mol%	V (μL)	Reaction time (h)
1	12.20	1-hexanol	1:19	2.00	None	–	–	24
2	12.20	1-hexanol	1:19	2.00	HCl	2	26.2	24
3	12.15	1-hexanol	1:19	2.00	$NaOCH_3$	0.2	6.0	24
4	4.85	1-hexanol	1:19	0.80	$NaOCH_3$	2	24.2	24
5	12.20	1-hexanol	1:19	2.00	$NaOCH_3$	20	600	24
6	12.20	1-hexanol	1:19	2.00	$NaOCH_3$	0.2	6	1
7	12.15	1-hexanol	1:19	2.00	$NaOCH_3$	2	60	1
8	11.95	1-hexanol	1:19	2.00	$NaOCH_3$	10	302	1
9	5.80	1-hexanol	1:9	2.00	$NaOCH_3$	2	60	24
10	2.50	1-hexanol	1:4	2.00	$NaOCH_3$	2	60	24
11	12.15	1-hexanol	1:19	2.00	$NaOCH_3$	2	60	10
12	12.15	1-hexanol	1:19	2.00	$NaOCH_3$	2	60	6
13	12.15	benzyl alcohol	1:19	1.65	$NaOCH_3$	2	60	10
14	12.15	cinnamyl alcohol	1:19	2.05	$NaOCH_3$	2	60	10
15	12.15	2-(hydroxymethyl) pyridine	1:19	1.55	$NaOCH_3$	2	60	10

[a] The Au/substrate ratio was 1:625 in all experiments. The autoclave was pressurized to a total pressure of 10 bar (corresponding to a O_2 pressure of 9.2 bar) in all experiments except for the Entry 2 experiment where a total pressure of 4 bar was used (O_2 pressure 3.2 bar). The O_2/substrate ratio was 7:1 in all experiments.
[b] Substrate: methanol molar ratio.

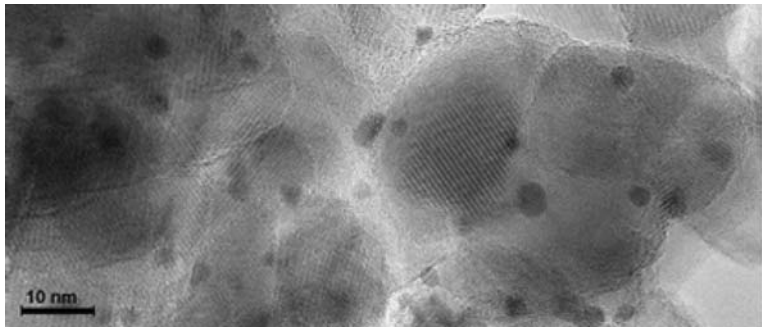

Figure 3. Representative transmission electron microscopy image of the Au/TiO_2 catalyst, showing mainly the presence of nanosized gold particles with a size of 2–5 nm.

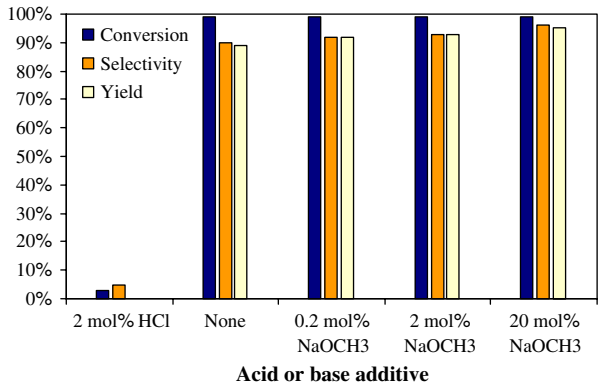

Figure 4. Effect of acid or base additives on the yield of methyl hexanoate at full conversion.

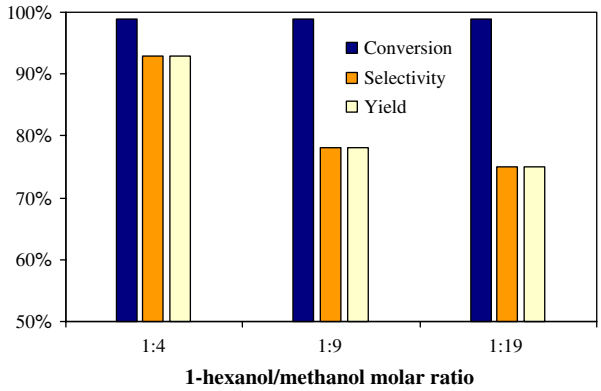

Figure 5. Effect of substrate/methanol ratio on the yield of methyl hexanoate.

be produced in excellent yield, even under neutral conditions. However, although presence of base is not essential for the reaction, it does have a pronounced influence on the reaction rate, as shown in table 2. Thus, to conduct the reaction at short reaction times, the desired amount of base can be added. This could be particularly important for alcohols that can isomerise or possibly even degrade under the reaction conditions. However, it might in many cases be desirable to avoid the use of base to ease purification and minimize waste.

GC-analysis of the reaction mixtures after neutralization with aqueous hydrochloric acid show that small amounts of formic acid, and very minute amounts of hexanoic acid are formed. For the Entry 4 experiment (see table 1), for instance, the neutralized reaction mixture contained *ca.* 2% of formic acid and less than 0.3% of hexanoic acid. Generally, the only major byproduct in these reactions result from the condensation of the oxidized alcohol with the substrate alcohol. No Claisen condensation products were observed in the reaction mixtures. GC analysis of the gas mixture after conducting the Entry 5 experiment (see table 1) showed that the gas mixture after reaction consisted of 78% CO_2, suggesting that some methanol is oxidized to CO_2 during the reaction. In all, the excess of O_2 present in the autoclave after the reaction corresponds to a maximum loss of 1–3 moles of methanol per mole of methyl ester formed, this methanol being oxidized to either formic acid, methyl formate or to CO_2.

Figure 5 shows the effect of the hexanol/methanol ratio on the yield of methyl hexanoate. These experiments were all conducted using 2% $NaOCH_3$ with a reaction time of 24 h. As is evident, the selectivity towards the methyl ester increases when increasing the

Table 2
Effect of base on reaction rate

Entry in Table 1	Substrate	Reaction time (h)	$NaOCH_3$ additive (mol%)	Product	Conv. (%)	Yield (%)
6	1-hexanol	1	0.2	methyl hexanoate	56	52
7	1-hexanol	1	2	methyl hexanoate	60	57
8	1-hexanol	1	10	methyl hexanoate	85	81

Table 3
Results obtained for the experiments with lowering of the reaction time in the oxidation of 1-hexanol

Entry in Table 1	Substrate	Reaction time (h)	$NaOCH_3$ additive (mol%)	Product	Conv. (%)	Yield[a](%)
4	1-hexanol	24	2	methyl hexanoate	>99	93
11	1-hexanol	10	2	methyl hexanoate	97	93 (79)
12	1-hexanol	6	2	methyl hexanoate	96	91

[a] The yield in parenthesis is the isolated yield.

Table 4
Results obtained for the experiments with oxidizing various primary alcohols to yield methyl esters

Entry in Table 1	Substrate	Reaction time (h)	$NaOCH_3$ additive (mol%)	Product	Conv. (%)	Yield[a](%)
13	benzyl alcohol	10	2	methyl benzoate	>99	>99 (79)
14	cinnamyl alcohol	10	2	methyl cinnamate	>99	88 (76)
15	2-(hydroxymethyl) pyridine	10	2	methyl pyridine- 2-carboxylate	95	95 (85)

[a] The yields in parenthesis are the isolated yield.

excess of methanol. This trend is most likely caused by the more favored formation of the methyl hemiacetal compared to the hexyl hemiacetal. However, good yields of methyl hexanoate (75%) can still be obtained by using a substrate/methanol ratio of just 1:4. Thus, the selection of substrate alcohol/methanol ratio obviously represents a compromise between maximizing the yield and making the separation as easy as possible since at high methanol concentrations the separation of the product is more energy and time-consuming. Furthermore, the reaction is obviously slower when it is conducted at high dilution. However the separation is generally very simple since the methyl esters are usually recovered in high yields by a straightforward distillation.

Then we investigated the importance of the reaction time. The results of these experiments are listed in table 3. It is seen, that the reaction time can easily be reduced from 24 to 10 h or even to 6 h since nearly full conversion and an excellent selectivity towards the methyl ester is achieved after only 6 h. However, the yield is still slightly higher when the longer reaction times are used. This is because no loss of selectivity is observed at full conversion.

We also investigated the versatility of this new methodology by carrying out oxidations of other substrates than 1-hexanol. These results are shown in table 4, and it is seen that the method is quite versatile since both benzyl alcohol, cinnamyl alcohol, and 2-(hydroxymethyl)pyridine can be oxidized to the corresponding methyl esters in good to excellent yields. Thus, an amine functionality does not deactivate the gold catalyst. However, the highly sterically demanding 1-adamantane methanol fails to undergo oxidation. Also for these substrate, GC-analysis of the reaction mixtures after neutralization with aqueous hydrochloric acid show that small amounts of formic acid, and very minute amounts of carboxylic acid are formed. However, in the oxidation of cinnamyl alcohol, *ca.* 10% of methyl benzoate was formed as a by-product.

4. Conclusions

In conclusion, we have presented here a new application in the field of gold catalysis with the direct formation of methyl esters from various primary alcohols, using O_2 as oxidant. Importantly, the primary alcohols are evidently oxidized much more readily than methanol. It must be noted, however, that no attempts have so far been made to optimize the reaction conditions and thereby reduce the methanol loss during reaction, although this work is underway.

Acknowledgments

The Center for Sustainable and Green Chemistry is sponsored by the Danish National Research Foundation.

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DOI: 10.1002/cssc.200700033

Chemicals from Renewables: Aerobic Oxidation of Furfural and Hydroxymethylfurfural over Gold Catalysts

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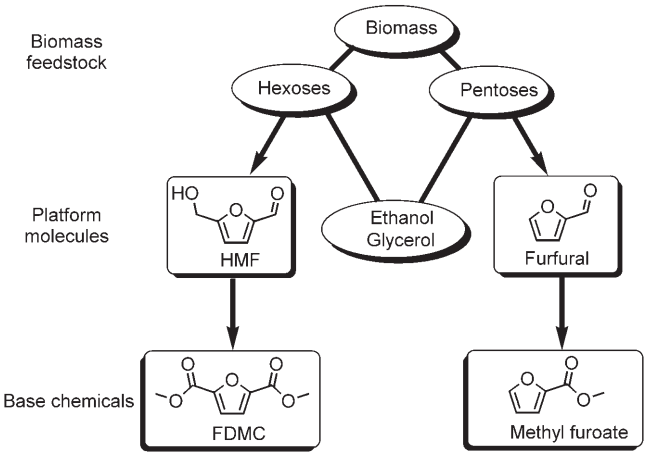
In recent years, there has been a significantly increasing focus on the development of technologies that facilitate the conversion of biorenewables into transportation fuels.[1–3] Sustainable transportation fuels have received considerable political focus, partly due to long-term environmental concerns but also because of the dramatic effects of oil prices on the global economy.[1] Today, about 95% of all manufactured chemicals originate from fossil resources. As oil prices fluctuate and the demand for fossil resources grows, the price of commodity base chemicals will follow. A shift from conventional petrochemical feedstocks towards biomass feedstocks for the production of commodity base chemicals would ensure stable prices and, therefore, seems attractive. The Roadmap for Biomass Technologies in the U.S. predicts that by the year 2020, 18% of all manufactured chemicals will originate from biomass.[4] Unfortunately, the vision of a chemical industry based partly on a renewable biomass feedstock is impeded by the availability of technology for converting biomass into important platform molecules, which are envisaged as key building blocks in the future chemical industry, as well as the technology for converting platform molecules into renewable base chemicals.

Here, we show that oxidative esterification of platform molecules such as hydroxymethylfurfural (HMF) can be an effective route in the conversion of platform molecules into renewable base chemicals, which can be used, for example, as polymer building blocks, by the use of only the simplest reagents such as oxygen and methanol.

Biorefineries convert raw biomass into sugar monomers such as glucose, fructose, and xylose, which can be fermented to platform molecules like ethanol and glycerol (Scheme 1). Transformation of sugar monomers into renewable base chemicals by traditional chemical means, such as heterogeneous catalysis, is a research area still in its infancy. However, recently this area has seen significant improvements. Glucose has, for instance, been hydrogenated to form alkanes and catalytically reformed to form CO and hydrogen.[2,5] Fructose and xylose are known to dehydrate under acidic conditions to form HMF and furfural in high yields. Glucose, on the other hand, tends to form numerous by-products under similar conditions. However, very recently Dumesic and co-workers have shown that glucose and even starch can be dehydrated to HMF in moderate yields by the use of a biphasic solvent system, paving the way for an economically feasible conversion of biomass into chemically derived platform molecules.[6] As the production of polymers consumes the largest proportion of petrochemical feedstocks used in the chemical industry,[7] the development of new routes to this class of chemicals represents some of the major challenges in the shift from petrochemical to biorenewable feedstocks. In this respect, HMF plays a vital role as it can be oxidized to 2,5-furandicarboxylic acid (FDCA), which has been proposed as a replacement for terephthalic acid used as a monomer in polyethylene terephthalate (PET) plastic.[8]



Scheme 1. Biomass feedstocks can be transformed into platform molecules by chemical means or fermentation. By oxidative esterification of HMF, the polymer building block furan-2,5-dimethylcarboxylate (FDMC) can be obtained. Analogously, furfural can be transformed directly into methyl furoate, which is used in the fine-chemical industry.

FDCA has been formed by aerobic oxidization of HMF with platinum on alumina by continuous addition of a stoichiometric amount of base.[9] A homogeneous catalytic system comprising several transition-metal acetates and a bromide source in acetic acid has been shown to form FDCA in moderate yields with the use of air as the oxidant.[10] More recently, fructose has been converted into FDCA in good yields through in situ dehydration to HMF, followed by oxidation with a supported cobalt catalyst and air.[11]

In the past two decades, gold has revealed itself to be an excellent catalyst for selective oxidations with molecular oxygen when distributed in the form of nanoparticles[12–19] and thereby offers an alternative to other "green" oxidation catalysts.[20–22] Gold has, for example, been used to oxidize aqueous ethanol to form acetic acid,[23] illustrating the concept of converting platform molecules into renewable base chemicals. Other examples involve the oxidation of glucose and glycerol under basic conditions to form gluconate and glycerate solutions.[24–27] Recently, we demonstrated that by oxidizing primary

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alcohols in methanol with the use of supported gold nanoparticles and air, methyl esters are formed directly in excellent yields.[28] This procedure circumvents the use of a stoichiometric amount of base because the product does not lower the pH value of the solution. Intrigued by the high efficiency of this procedure, we were interested to examine if biomass-derived platform molecules such as HMF and furfural can be converted directly into useful renewable base chemicals, thus opening up a new and alternative route in the utilization of biomass.

HMF dissolved in methanol (1:79 molar ratio) was oxidized to FDMC in a stirred, pressurized batch autoclave with a catalytic amount of gold on titania. A small amount of sodium methoxide (8%) was added, as base enhances the reaction rate of the oxidative esterification.[28] The autoclave was pressurized to 4 bar O_2 and placed in an oil bath at 130 °C for 1–3 h. The time-related conversion of HMF was examined by performing independent oxidation reactions and analyzing the product distribution at various time intervals by gas chromatography (Figure 1a).

The results show that HMF is oxidatively esterified to FDMC in excellent yield (98% yield by GC) in only 3 h. The gold catalyst can be recovered by filtration and reused, and the reaction mixture is worked up by removal of methanol to leave the crude FDMC as a beige solid. In contrast to FDCA, FDMC is easily purified by sublimation at standard pressure and 160 °C to afford colorless crystals. Hence, the workup procedure is very simple, and high-purity FDMC is easily obtained.

It can be seen from Figure 1 that the oxidation to form the diester proceeds by a series of consecutive reactions and that the slowest step is the oxidation of the alcohol moiety of HMF in agreement with recent findings for the oxidation of ethanol in water.[29] In the oxidation of ethanol, there was essentially no effect of changing the support from titania to spinel, and this suggests that the support does not play a direct role in the reaction.

By oxidizing HMF at room temperature with an oxygen pressure of just 1 atm, 5-hydroxymethyl methylfuroate (HMMF) is formed in excellent yield after only a few hours (Figure 1b). This result confirms that the aldehyde moiety of HMF is oxidized much faster than the hydroxymethyl group, hereby leading to initial formation of HMMF, as is also evident from Figure 1a. At higher temperatures, the hydroxymethyl group is further oxidized to the aldehyde, to form methyl 5-formyl-2-furoate (MFF) and finally oxidatively esterified to FDMC (Scheme 2). In the aerobic oxidations performed at room temperature, no oxidation of methanol is observed at all. At higher temperatures and at longer reaction times some methanol can be oxidized to carbon dioxide or formates (up to 0.4 mol per mole of substrate),[30] and thus it is important to optimize the reaction time.

These results are quite surprising as furan-2,5-dicarbaldehyde has been reported as the initial intermediate in the platinum-catalyzed oxidation of HMF in water.[9] In fact, in none of our experiments was furan-2,5-dicarbaldehyde observed in more than trace amounts, thereby supporting the observation that oxidation of HMF in methanol with gold nanoparticles

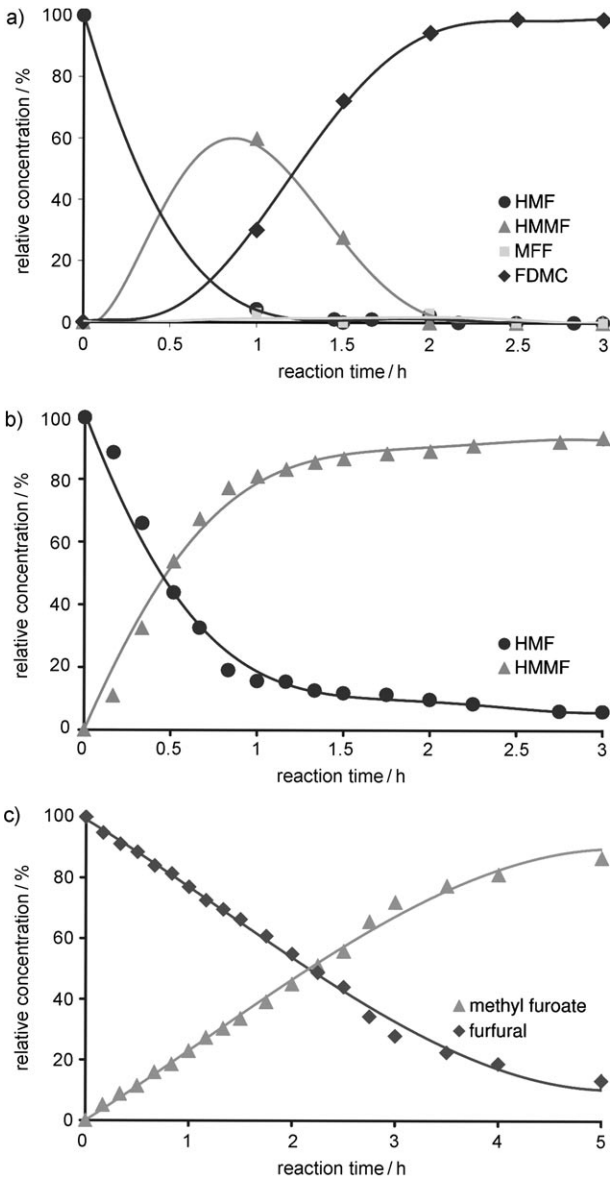
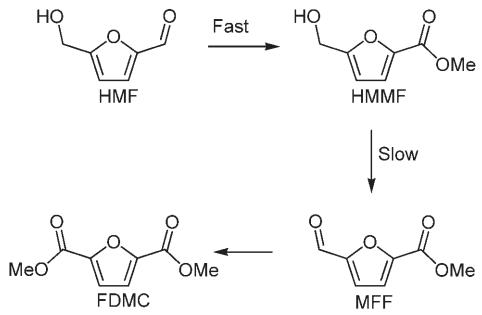


Figure 1. a) Oxidation of HMF to form FDMC. $p(O_2)$ 4 bar, 130 °C, Au/substrate 1:313, 8% methoxide relative to HMF. b) Oxidation of HMF to form HMMF. $p(O_2)$ 1 bar, 22 °C, Au/substrate 1:313, 8% methoxide relative to HMF. c) Oxidation of furfural to form methyl furoate. $p(O_2)$ 1 bar, 22 °C, Au/substrate 1:313, 8% methoxide relative to furfural. HMF and product ratios were determined by GC.



Scheme 2. Proposed oxidation pathway of HMF to FDMC. The hemiacetal intermediates are omitted for clarity.

occurs with a different chemoselectivity than that observed with platinum catalysts in water or that a very pronounced solvent effect exists. This reactivity difference might be ascribed to the fact that platinum catalysts typically exhibit much higher activity in dehydrogenation reactions than gold catalysts.

As second-generation biorefining gains ground, xylose could become an abundant resource. Xylose is easily converted into furfural, and thus we examined if furfural could be oxidatively esterified to methyl furoate. Furfural was oxidized in methanol at room temperature with 1 bar oxygen. Because the only functional group present is an aldehyde moiety, full oxidation to methyl furoate occurs under very mild reaction conditions (22 °C) in a relatively short time (Figure 1c; full conversion is achieved in 10–12 h). The formed methyl furoate can easily be purified by distillation. This offers a mild and efficient way to derivatize furfural with the use of oxygen as the only stoichiometric reagent.

Thus, in conclusion, HMF can be transformed directly into FDMC in the presence of gold nanoparticles and air in excellent yield. The oxidation occurs readily at 130 °C and does not require addition of a stoichiometric amount of base. FDMC is easily purified by low-temperature sublimation to give high-purity FDMC, which can be used as a monomer for replacement of terephthalic acid in plastics. Similarly, furfural can be transformed directly into methyl furoate, which is easily converted into compounds that find use as flavor and fragrance components in the fine-chemical industry. However, in the future much wider applications of methyl furoate may be envisaged, for example, as a cheap industrial solvent or extractant.

Experimental Section

In all experiments, a gold on titania (1 wt% Au) reference catalyst from the World Gold Council was used. The chemicals were used as received, without further purification. Gas chromatography (GC) was performed on an Agilent Technologies 6890N GC instrument equipped with a flame ionization detector (FID) and a HP-5 column (30 m × 0.320 mm × 0.25 μm, J&W Scientific, catalogue 19091J-413). NMR spectra were recorded on a Varian Mercury 300 MHz instrument. Chemical shifts were determined relative to that of chloroform ($\delta = 7.26$ ppm). Data were processed with MestReC 4.7.4.0 software.

Experiments conducted at 130 °C were performed as follows: A 325-mL titanium-stabilized T316 autoclave from the Parr Instrument Company was charged with Au/TiO_2 (0.25 g, 0.013 mmol Au), methanol (12.65 mL, 300 mmol), HMF (0.50 g, 4.0 mmol; >99%, SAFC), and 30 wt% solution of sodium methoxide in methanol (0.060 mL, 0.3 mmol). The autoclave was fitted with a magnet stirrer bar, flushed with oxygen, and pressurized with 4 bar O_2 (52 mmol). The autoclave was then heated in an oil bath at 130 °C for the desired reaction time. After reaction, the autoclave was cooled to room temperature and the reaction mixture was analyzed (GC) by dissolving all organic material with an excess of methanol. FDMC was isolated by removal of methanol under reduced pressure. The remaining beige solid was sublimed at 1 atm and 160 °C to afford colorless crystals. NMR spectroscopy confirmed that the product was FDMC: ^{1}H NMR (300 MHz, $CDCl_3$, 295K): $\delta = 3.92$ (6H), 7.21 ppm (2H); ^{13}C NMR: $\delta = 52.39$, 118.46, 146.57, 158.37 ppm.

Experiments conducted at room temperature (22 °C) were performed as follows: A two-necked 100-mL round-bottomed flask was charged with Au/TiO_2 (0.25 g, 0.013 mmol Au), methanol (12.65 mL, 300 mmol), HMF (0.50 g, 4.0 mmol; >99%, SAFC) or furfural (0.38 g, 4.0 mmol; >98%, Fluka), and 30 wt% solution of sodium methoxide in methanol (0.060 mL, 0.3 mmol). The flask was equipped with a rubber septum and a condenser and fitted with a magnetic stirrer bar. The flask was flushed with oxygen and kept under an oxygen atmosphere. The reaction mixture was then stirred vigorously, and samples of the reaction mixture were taken out with a syringe and then analyzed by GC and GC-MS.

Acknowledgements

The Center for Sustainable and Green Chemistry is sponsored by the Danish National Research Foundation.

Keywords: gold · heterogeneous catalysis · oxidation · platform chemicals · supported catalysts

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Received: June 4, 2007
Revised: September 9, 2007
Published online on December 4, 2007

Aerobic oxidation of aldehydes under ambient conditions using supported gold nanoparticle catalysts†

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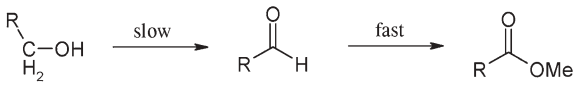
Received 8th August 2007, Accepted 14th November 2007
First published as an Advance Article on the web 26th November 2007
DOI: 10.1039/b712171g

A new, green protocol for producing simple esters by selectively oxidizing an aldehyde dissolved in a primary alcohol has been established, utilising air as the oxidant and supported gold nanoparticles as catalyst. The oxidative esterifications proceed with excellent selectivities at ambient conditions; the reactions can be performed in an open flask and at room temperature. Benzaldehyde is even oxidised at a reasonable rate below −70 °C. Acrolein is oxidised to methyl acrylate in high yield using the same protocol.

Over the past decade, the utilisation of gold catalysis has increased rapidly.[1] For a long time, gold was thought to be relatively inactive as a catalyst, but finally in 1973 it was shown to be active for the hydrogenation of olefins.[2] Later, the hydrochlorination of acetylene and the aerobic oxidation of carbon monoxide was reported by Hutchings[3] and Haruta *et al*,[4] respectively. Since that time, gold has been identified as the most active catalyst in a variety of reactions. Oxidations with molecular oxygen, in particular, have attracted increasing attention over recent years, since they represent "green" oxidation methods.[5] The oxidation of alcohol and aldehyde moieties using gold nanoparticles has previously been studied in some detail.[6–8]

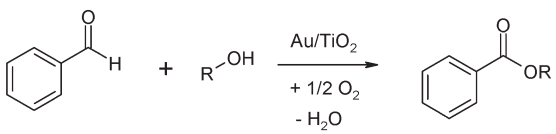
Herein, we show that supported gold nanoparticles can be used to catalyse the oxidation of benzaldehyde dissolved in different alcohols to directly produce various benzoate esters. The oxidising agent is air, a cheap and abundant resource. The experiments are conducted at room temperature, thus requiring no external heating, yielding an economic and practical route. The experiments take place in a flask open to air. It has been shown that if an alcohol is oxidised in the presence of a stoichiometric amount of aqueous base, carboxylates are achieved.[9] Base can in fact be negated from the starting reaction mixture, but then elevated temperatures are required to drive the reaction to full conversion. If the reactions are carried out in water, carboxylic acids result.[10,11] If performed in methanol, primary alcohols are converted into methyl esters.[12,13] For the latter process, only a catalytic amount of base is required. It has recently been established that the oxidation of alcohols to their corresponding methyl esters proceeds *via* an aldehyde intermediate. The rate determining step is believed to be dehydrogenation of the alcohol to form this aldehyde intermediate.[14] The second step—oxidation to form the methyl ester—proceeds relatively rapidly, indicated by the lack of accumulation of the aldehyde. This points to the possibility for aldehyde oxidations at much milder conditions than those used for alcohols. The reaction pathway can be seen in Scheme 1. Previous work on the oxidation of aldehydes to carboxylic acids has been conducted by Rossi *et al*.[15]



Scheme 1

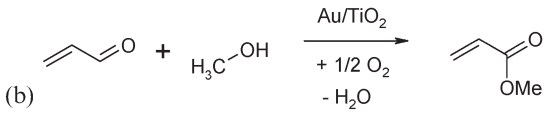
The catalytic reactions were carried out in an open glass flask, fitted with a condenser. All chemicals were used without further purification. NaOMe was used as a 30% solution in MeOH. In a typical experiment, gold supported on titanium dioxide (1% Au/TiO_2 supplied by Mintek) was suspended in the solvent alcohol. The aldehyde and base were added under stirring. Small aliquots were taken at selected times, the samples were filtered directly through a 13 mm syringe filter and analysed by GC and GC-MS. The GC column used was Agilent Technologies Inc. HP-5. For the acrolein reactions, a CP-PoraPLOT Q-HT column was used. The reaction equation for benzaldehyde is shown in Scheme 2a, and that for acrolein in Scheme 2b, which is considered later as an application of the method presented.

Fig. 1 shows the formation of methyl benzoate at varying temperatures. It can be seen that at decreasing temperatures the rate of formation of methyl benzoate decreases. The temperature is the limiting factor below 25 °C. Above this temperature it can be seen that there is no difference in the rates of reactions, implying that a factor other than temperature in now the rate determining factor. This could be the availability of atmospheric oxygen; we



R = CH_3, CH_2CH_3, $(CH_2)_2CH_3$, $(CH_2)_3CH_3$, $CH_2(C_6H_5)$

(a)



(b)

Scheme 2

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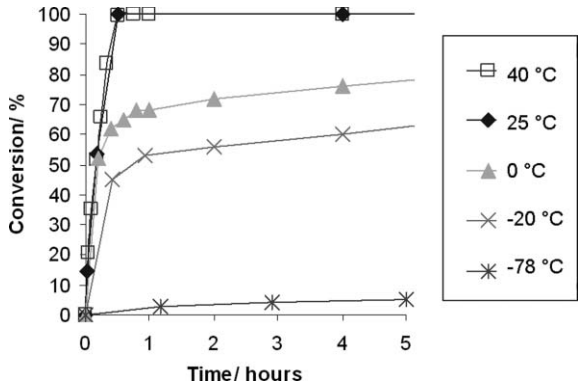

Fig. 1 Rate of formation of methyl benzoate at selected temperatures. *Reaction conditions*: Benzaldehyde : methanol 1 : 30, 0.2 mol% 1 wt% Au/TiO_2 from Mintek, 10 mol% 30% NaOMe soln. in MeOH.

would expect approximately the same amount of oxygen to be dissolved in the solution at 25 °C as at 40 °C, thus accounting for the similar reaction rates.[16]

Methyl benzoate can be formed from benzaldehyde at temperatures as low as −78 °C, proving this to be a facile and extremely fast reaction at room temperature. The remarkable catalytic activity of gold nanoparticles for aerobic oxidation of benzaldehyde at −78 °C was verified in an independent series of experiments. At these reaction conditions, *ca.* 2.7 mmol benzaldehyde was oxidized per mmol gold per hour.

Fig. 2a depicts the effect on the reaction rate of varying the amount of base present. Sodium hydroxide can also be utilised as

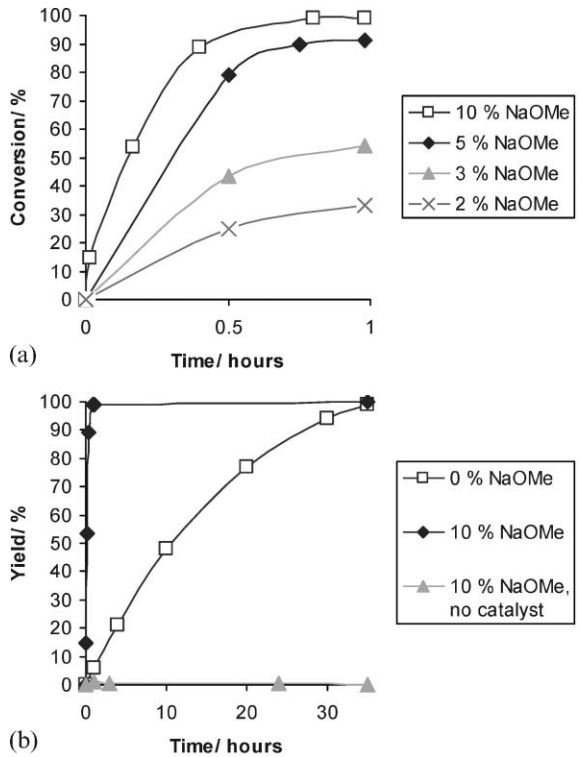

Fig. 2 a. Rate of formation of methyl benzoate with various amounts of base present. b. Conversion of benzaldehyde to methyl benzoate with no base present. *Reaction conditions*: Benzaldehyde : methanol 1 : 30, 0.2 mol% 1 wt% Au/TiO_2 from Mintek, T = 25 °C.

the base, but sodium methoxide was selected for practical purposes. A higher percentage of base yields a substantially faster reaction. With lower quantities of base the reaction takes longer to go to completion. Fig. 2b shows the results for formation of methyl benzoate in the absence of base. Formation of methyl benzoate with 10% base present is shown alongside for comparison. The fact that product formation occurs in excellent yield and selectivity even without base indicates that the protocol can be easily modified to the conditions required in special cases. Temperature, base presence and amount, and the use of oxygen or air as the oxidant can be varied, and full conversion with good to excellent yields are obtained; hence this can be viewed as a versatile and practical process. Furthermore, the reaction was run without catalyst (Fig. 2b), highlighting the necessity of the supported nanoparticles.

The protocol for methyl ester formation was investigated to study more generally ester formation. A range of simple alkyl alcohols and benzyl alcohol were utilised in place of methanol (Fig. 3). Formation of the methyl ester is by far the most rapid. On utilisation of longer chained alcohols, the rate of reaction decreases. This can be observed in the decreasing reaction rates of the alkyl alcohols, progressing from methanol to 1-butanol. When benzaldehyde is reacted with benzyl alcohol, the reaction rate is slower than that observed for methanol, but more rapid than for the alkyl alcohols. However in all cases, the reaction conditions can be tuned to produce the desired ester in high yield. Moreover, analogous experiments with hexanal and 2-methyl pentanal showed that it is also possible to achieve the corresponding methyl ester from these substrates in yields above 90%. However, full conversion is only reached after about 10 h showing that these aliphatic substrates are oxidized more slowly than benzaldehyde.

Further experimentation on the protocol set out above was executed using acrolein as the aldehyde starting material. Acrolein can be obtained from glycerol by dehydration at high temperatures,[17] and subsequently oxidised in methanol to furnish the methyl ester, methyl acrylate. Glycerol, as a by-product from biodiesel formation, is a very cheap and abundant feedstock.[18] Acrylate esters constitute an important group of feedstocks, for example, they are used to make water-based paints, solvent-based coatings and acrylic coatings. Our methodology enables such

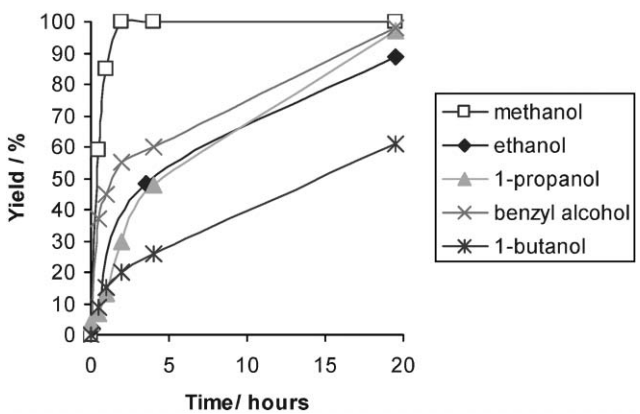

Fig. 3 Gold catalysed oxidation of benzaldehyde in alcohol solvent. *Reaction conditions*: Benzaldehyde : methanol 1 : 30, 0.2 mol% 1 wt% Au/TiO_2 from Mintek, T = 25 °C, 20 mol% 30% NaOMe soln. in MeOH.

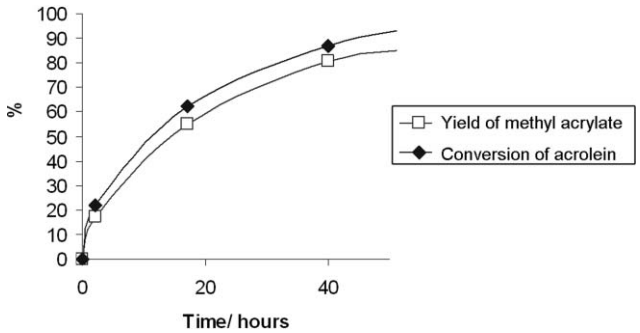

Fig. 4 Gold catalysed oxidation of acrolein in methanol. *Reaction conditions*: Acrolein : methanol 1 : 80, 0.9 mol% 1 wt% Au/ZnO from Mintek, T = 25 °C. Yield of methyl acrylate is shown.

acrylate esters to be synthesised, at room temperature, using air as the oxidant, thus providing a "green" route to methyl acrylate.

Methyl acrylate was synthesised from acrolein by the present aerobic oxidation protocol with 87% selectivity at 97% conversion (Fig. 4 and Scheme 2b). This result is achieved with no optimisation, thus providing a good yield of methyl acrylate at this stage.

In conclusion, we have described a practically, and potentially economically, very attractive route to furnish esters from aldehydes. The simplest available oxidant, air, is used and the oxidative esterifications run to full conversion with good to excellent selectivities. The oxidation reactions even take place at −78 °C, demonstrating the highly catalytic ability of gold nanoparticles. The methodology can be tuned to allow for varying temperatures and amounts of base, depending on the required reaction conditions. In addition, we have synthesised methyl acrylate from acrolein using the same advantageous process, and the scope for synthesising other acrylate esters by the same method stands as a strong possibility.

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Oxidation of glycerol and propanediols in methanol over heterogeneous gold catalysts†

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Received 17th September 2007, Accepted 21st December 2007
First published as an Advance Article on the web 17th January 2008
DOI: 10.1039/b714292g

Aerobic oxidation of glycerol over metal oxide supported gold nanoparticles in methanol results in the formation of dimethyl mesoxalate in selectivities up to 89% at full conversion. The oxidative esterification takes place in methanol, acting both as solvent and reactant, and in the presence of base. Thus, it constitutes a direct transformation of the glycerol by-product phase from biodiesel production or from glycerol obtained *e.g.* by fermentation. Au/TiO_2 and Au/Fe_2O_3 was found to have similar catalytic activity, whereas Au/C was inactive. 1,2-Propanediol was oxidized to methyl lactate with a selectivity of 72% at full conversion, while 1,3-propanediol yielded methyl 3-hydroxypropionate with 90% selectivity at 94% conversion. Methyl 3-hydroxy propionate can be easily converted into methyl acrylate, which is then a green polymer building block.

Introduction

The conversion of glycerol into high-value chemicals is a research area that has received tremendous attention in recent years.[1] This interest is spurred by the emergence of glycerol as an abundant renewable resource, formed as a by-product from the rapidly growing biodiesel production. Alternatively, glycerol can be obtained at relatively low cost by fermentation of glucose. Glycerol, being a highly functionalized compound, is difficult to convert selectively into useful chemical products. Recently, however, several good examples have been reported. One approach is the fermentation of glycerol to form 1,3-propanediol, which can be polymerized with terephthalic acid and used in the fibers industry.[2] Steam reforming of glycerol to form syn-gas coupled with a Fischer–Tropsch process to form hydrocarbon fuels is another possible approach to valorize glycerol and improve the overall efficiency of biodiesel production.[3] Glycerol has recently been dehydrated over a copper-chromite catalyst to form 1-hydroxyacetone in high yields, which upon hydrogenation gives 1,2-propanediol that can be used as a replacement for ethylene glycol in anti-freeze applications.[1,4] Dehydration over an acidic zeolite catalyst can furnish acrolein with high selectivities,[5] thus illustrating the possibilities of producing bulk chemicals from biomass.

Here, we report that oxidation of glycerol in methanol over supported gold catalysts results in the formation of dimethyl mesoxalate in 89% selectivity at full conversion. The major by-product formed is methyl glycolate, resulting from C–C cleavage of intermediary products. 1,2-Propanediol and 1,3-propanediol, which are both available from glycerol, are also examined as starting materials for the oxidative esterification. 1,2-Propanediol is oxidized to furnish methyl lactate with a selectivity of 72% at full conversion. Here, methyl acetate is formed as the major by-product. 1,3-Propanediol is oxidized to form methyl 3-hydroxypropionate as the major product with 90% selectivity at 94% conversion.

Selective oxidation could play a prominent role in the conversion of glycerol if the oxidizing agent used is oxygen. Kimura *et al.* have reported that aerobic oxidation of glycerol over a carbon supported Pt–Bi catalyst yields dihydroxyacetone in selectivities up to 80%.[6] Oxidation of glycerol over Pd/C under basic conditions have been reported by Besson and co-workers to give glyceric acid with 70% selectivity at full conversion.[7]

Supported gold nanoparticles[8,9] have been found to be excellent catalysts for the oxidation of various substrates such as CO,[10] propylene,[11] hydrogen,[12] primary and secondary alcohols,[13–16] aldehydes[17] and even cyclohexane[18,19] and alkenes.[20] Oxidation of diols and glycerol in water has also been studied extensively.[13,21–30] The interesting finding in this research area is that under the right circumstances, Au can be more active and selective towards glyceric acid than Pd and Pt. Indeed, Hutchings and co-workers have reported glyceric acid selectivities of 100% at 56% conversion.[22] Further oxidation of glyceric acid leads to formation of tartronic acid, and in some cases C–C cleavage to form glycolic acid, oxalic acid and CO_2 is observed.[23–25] Various supports have been examined, and carbon supported catalysts appear to be of superior activity compared to metal oxide supported catalysts.[13,26] Another parameter of crucial importance is the gold nanoparticle size.[21,23,25] Very recently, Davis and co-workers examined the rate of glycerol oxidation using gold nanoparticles with varying sizes. Small gold nanoparticles (5 nm) were found to be much more active than larger particles (20 nm). However, higher selectivity towards glyceric acid was

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† This paper was published as part of the themed issue of contributions from the 3rd International Conference on Green and Sustainable Chemistry.

achieved with large sized gold nanoparticles.[25] The pH value of the reaction mixture is also an important reactivity parameter. Gold catalyzed oxidation of glycerol does not take place in the absence of base, and since the formation of glyceric acid will lower the pH as it is formed, it is necessary to maintain a high pH level by addition of sodium hydroxide.[12,23] Thus, a stoichiometric amount of sodium hydroxide is required when glycerol is oxidized to glyceric acid, usually as much as four equivalents of base is used to achieve a reasonable reaction rate. Recently, it was reported that by oxidizing a primary alcohol over a gold catalyst in methanol, methyl esters are formed instead of carboxylic acids.[27–29] In this procedure, base also promotes the catalytic activity. However, the methyl ester product does not consume base, and thus a small amount of base is capable of promoting the reaction. Since glycerol produced as a byproduct from biodiesel production is directly formed as a base-containing methanol solution, oxidation of this waste stream could offer an extremely simple route to new chemicals from biomass.

Experimental

Materials

Glycerol (>99%) was acquired from H. Struers Chemical Labs, methanol (>99.9%), 30 wt% sodium methoxide in methanol, 1,2-propanediol (>99%) and 1,3-propanediol (>99%), anisol (>99%), 1-hydroxyacetone (90%), methyl lactate (99%), methyl pyruvate (95%), methyl acrylate (>99%), and dimethyl malonate (>99%) were all acquired from Sigma-Aldrich. 5 wt% Titanyl sulfate (aqueous sulfuric acid solution) was from Fluka (highest purity). Technical air (20% O_2, 80% N_2) was from Air Liquide.

Gold catalysts, Au/C, Au/TiO_2, Au/Fe_2O_3, were supplied by the World Gold Council (WGC).[30]

Catalyst characterisation

0.8% Au/C (X40S, type D catalyst from WGC) was prepared by the colloidal method. The average Au diameter was found to be 10.5 nm by TEM analysis and 6.7 nm with XRD.

Au/TiO_2 (type A catalyst from WGC, Lot No. #02-6) has 1.0 wt% Au and was prepared by the deposition–precipitation method. The average Au particle diameter was found to be 3.5 nm by TEM observation, with a standard deviation of 0.91 nm.

Au/Fe_2O_3 (type C catalyst from WGC, Lot No. #02-5) has 1.0 wt% Au and was prepared using the co-precipitation method. TEM observation revealed that the Au particle diameter on average is 3.6 nm, with a standard deviation of 0.65 nm.

Oxidation experiments

The oxidation experiments are performed in a 50 ml steel autoclave (MicroClave from Autoclave Engineers). The autoclave is charged with 250 mg of glycerol (2.7 mmol) and 5.1 g of methanol (159 mmol). 29 mg of 30 wt% $NaOCH_3$ in methanol is added (0.27 mmol) together with 30 mg of anisol (0.28 mmol, internal standard). Then the 1% Au/TiO_2 catalyst is added (0.48 g, 0.024 mmol Au) and the autoclave is sealed and pressurized to 21 bar with technical air (*ca.* 8 mmol O_2). The mixture is stirred (900 rpm) and heated to 373 K. At regular intervals, the autoclave is cooled to 263 K, and a sample is taken out. The autoclave is then recharged with technical air, and reheated to 373 K. In this way, the time-dependencies of the oxidation of the polyols are mapped by plotting the concentrations of reactants and products to establish possible reaction routes. Without a regular refilling of the autoclave with a fresh air atmosphere, the reaction proceeds at a significantly lower rate.

Oxidations of 1,2-propanediol and 1,3-propanediol are performed analogously by using 210 mg of each, corresponding to 2.7 mmol. Furthermore, oxidation of 1,2-propanediol is performed using 0.96 g of 1% Au/TiO_2 catalyst.

Product analysis

The reaction mixtures were analyzed by GC (Agilent Technologies 6890N, the column was an HP-5 from J & W Scientific, 30 m long and a diameter of 0.32 mm, and has an inner film of 0.25 μm 5% methyl phenyl siloxane) and GC-MS (Shimadzu Spectachrom QP5000 GC-MS, the column was Supelco Equity-1 of 30 m in length, an inner diameter of 0.25 mm and an inner film of dimethyl polysiloxane).

Reference samples were used to confirm the products whenever possible. However, the oxidation products dimethyl tartronate and methyl-3-hydroxypropionate could not be obtained and identification was thus conducted on the basis of MS data.‡

Quantifiable product data was obtained from GC, and were calculated on the basis of an internal standard. The concentration change due to methanol consumption in the oxidative esterification is ignored in the calculation of product concentrations.

Hydrogen peroxide formation and decomposition was determined by absorbance measurement of the H_2O_2–titanyl complex§ at 412 nm using a Jasco V-570 UV/VIS/NIR spectrophotometer.

Results and discussion

Oxidation of glycerol

Glycerol was oxidized in a stirred batch autoclave at 373 K in the presence of 10% sodium methoxide in methanol. Au/C

‡ Methyl glycerate was generated *in situ* by dissolving sodium glycerate (>99% from Sigma-Aldrich) in methanol and adding a small excess of 18 M sulfuric acid and heating to 60 °C for one hour. Dimethyl mesoxalate is not commercially available. However dissolving commercially available diethyl mesoxalate (>95%, Sigma-Aldrich) in methanol in the presence of base affords dimethyl mesoxalate and ethanol. On basis of these procedures it was possible to acquire reference data of the retention times of methyl glycerate and dimethyl mesoxalate.

§ H_2O_2 decomposition over Au/Fe_2O_3 and Au/TiO_2 was determined by adding 0.52 g of 33% H_2O_2 to a 60 °C hot suspension containing methanol (10 ml), sodium methoxide (0.19 mmol) and gold catalyst (100 mg). Samples (0.2 ml) of the reaction mixture were centrifuged, acidified and added to a solution containing 0.025 mmol $TiO(SO_4)$ in 2 ml sulfuric acid (5.5 M). The concentration of the formed H_2O_2–titanyl complex was determined by UV-VIS absorption and is proportional to the amount of hydrogen peroxide in the sample. After 5 minutes it was found that Au/Fe_2O_3 had decomposed 82% of the H_2O_2, while Au/TiO_2 had only decomposed 70%. This procedure was also used to identify the presence of H_2O_2 in the reaction mixture from oxidation of glycerol (H_2O_2 was not found in an unreacted sample).

has previously been reported as a highly active catalyst for oxidizing glycerol, and most reports on gold-catalyzed oxidation of glycerol use Au/C as catalyst.[22–26,31] Oxidation of glycerol in methanol by the use of carbon supported gold nanoparticles (10.5 nm) did not result in any conversion of glycerol. The lack of reactivity for the Au/C catalyst is likely due to the large size of the gold nanoparticles since smaller gold nanoparticles (3.5 nm) on Au/TiO_2 and Au/Fe_2O_3 were found to be able to oxidize glycerol. Thus, the oxidation of glycerol was investigated by using these two metal oxide supported catalysts.

The oxidation reaction was followed by GC and the concentration of the reaction products is plotted against time (Fig. 1 and 2). When either Au/TiO_2 or Au/Fe_2O_3 was used, methyl glycerate is the initially observed product. However, oxidation of glycerol must first lead to formation of dihydroxyacetone or glyceraldehyde, which are tautomers and in equilibrium under basic conditions. Thus, both intermediates can lead to methyl glycerate *via* oxidation of the glyceraldehyde hemiacetal (Scheme 1). However, none of these species were seen by GC, suggesting that they are rapidly converted into methyl glycerate. After a few hours, the concentration of methyl glycerate drops. This is caused by further conversion of methyl glycerate into dimethyl tartronate. Formation of dimethyl tartronate must be preceded by oxidation of methyl glycerate into methyl 3-hydroxy 2-oxopropionate or methyl 2-hydroxy-3-oxopropionate, which are also tautomers and in equilibrium under basic conditions. Final oxidation of dimethyl tartronate proceeds rapidly to furnish the fully oxidized dimethyl mesoxalate.

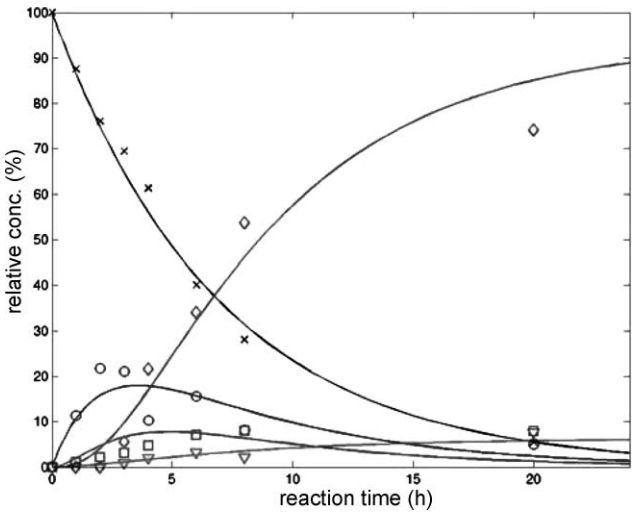


Fig. 1 Glycerol: –×–, methyl glycerate: –○–, dimethyl tartronate: –□–, dimethyl mesoxalate: –◇–, methyl glycolate: –▽–. Oxidative esterification of glycerol with the use of 1% Au/TiO_2. Methanol : glycerol was 59 : 1, Au : glycerol was 1 : 112. $T = 373$ K, $p(O_2) = 5.0$ bar. 10% $NaOCH_3$ relative to glycerol was used.

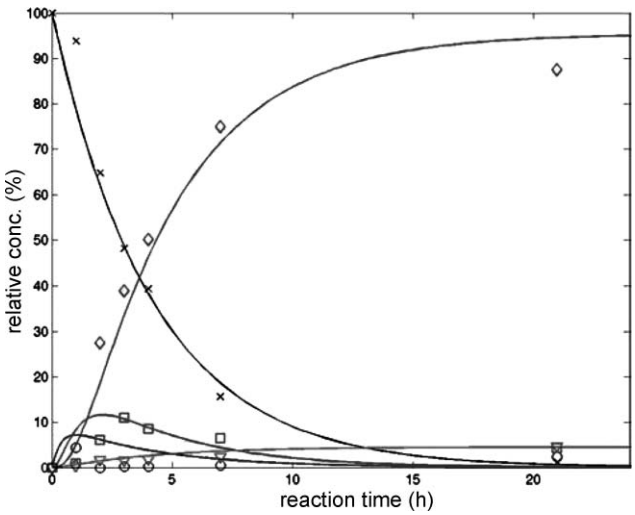


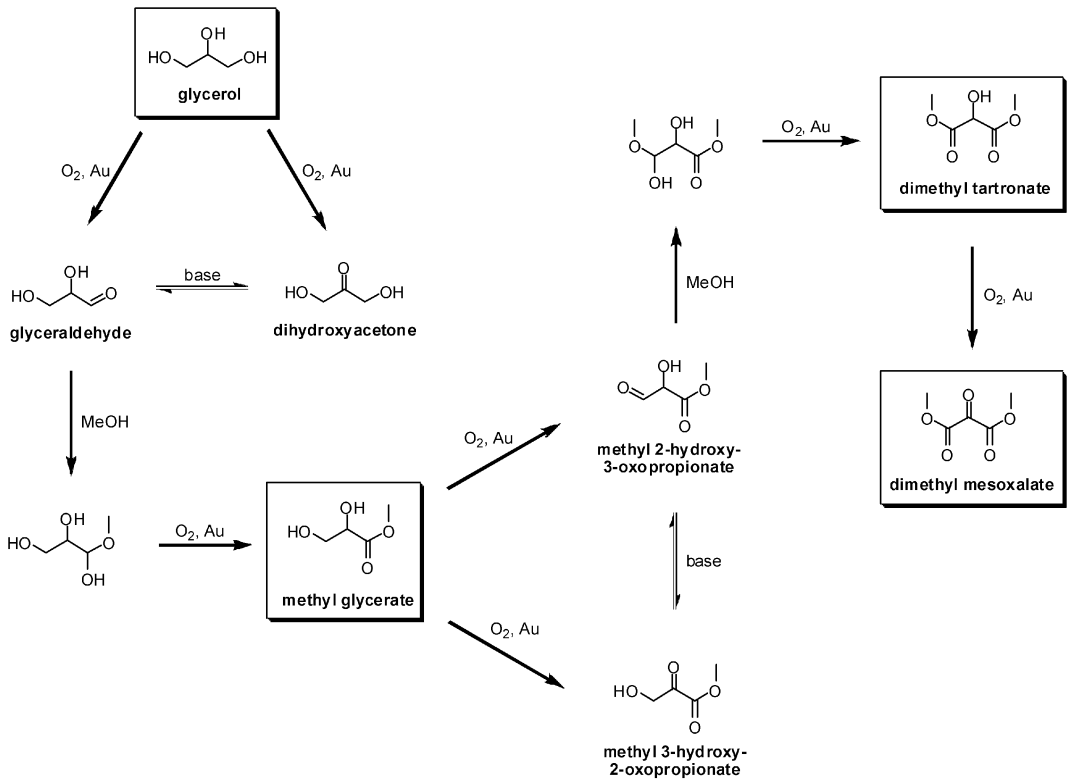
Fig. 2 Glycerol: –×–, methyl glycerate: –○–, dimethyl tartronate: –□– dimethyl mesoxalate: –◇–, methyl glycolate: –▽–. Oxidative esterification of glycerol with the use of 1% Au/Fe_2O_3. Methanol : glycerol was 59 : 1, Au : glycerol was 1 : 112. $T = 373$ K, $p(O_2) = 5.0$ bar. 10% $NaOCH_3$ relative to glycerol was used.

Methyl glycolate was also produced in minor quantities. This by-product results from C–C cleavage of a C3 unit during the reaction. This C–C cleavage could be thought to originate from a retro aldol reaction of methyl tartronate to form methyl 2-hydroxyacetate and dimethyl carbonate. However, dimethyl carbonate was never observed in the reaction mixture. Furthermore, it has recently been established that there is a close correlation between the formation of hydrogen peroxide and the amount of C–C cleavage observed when oxidizing glycerol in water with gold and gold–palladium particles.[25,31] It is thus likely that the same correlation is found in methanol and that hydrogen peroxide cleaves a C–C bond in either dihydroxyacetone, methyl glycerate or dimethyl tartronate, thus forming methyl glycolate. Analysis of the reaction mixture during oxidation of glycerol in methanol established that a low concentration of hydrogen peroxide is indeed present. Hydrogen peroxide is known to form when oxidizing substrates such as CO and glycerol in water over gold catalysts.[31] As water is inevitably present in the reaction mixture as a byproduct from the aerobic oxidation, hydrogen peroxide is likely to be formed in a similar fashion. Interestingly, methyl glycolate does not undergo further oxidation to form dimethyl oxalate. This selectivity has also been observed by Hayashi *et al.*[27]

Oxidation of glycerol over Au/Fe_2O_3 occurs with higher rate and selectivity than over Au/TiO_2 (Fig. 2). Thus, a 50% conversion of glycerol is achieved within 3 hours. The intermediates are formed in the same order, suggesting the same reaction mechanism. However, methyl glycerate is consumed faster over Au/Fe_2O_3 than over Au/TiO_2. The final product, dimethyl mesoxalate is formed with a higher selectivity (89%) over Au/Fe_2O_3 than when using Au/TiO_2 (79%) The higher selectivity is likely attributed to the finding that the Au/Fe_2O_3 catalyst is better at decomposing hydrogen peroxide than Au/TiO_2, thereby reducing the amount of C–C cleavage induced by hydrogen peroxide.§

Oxidation of 1,2-propanediol

It has been reported that 1,2-propanediol is oxidized more slowly than glycerol over gold catalysts.[21,26] We observed the same trend. However, by increasing the catalyst loading it is possible to achieve full conversion within a short time-frame (Fig. 3). Thus, after one hour, the conversion of 1,2-propanediol is 87%, and the two major products at this stage are methyl lactate and



Scheme 1 Reaction scheme for oxidative esterification of glycerol in the presence of base. Observed products are highlighted in boxes.

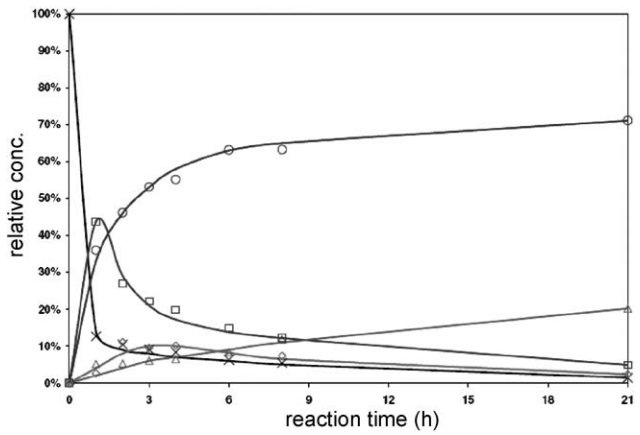


Fig. 3 1,2-Propanediol:–×–, methyl lactate:–○–, 1-hydroxyacetone:–□–, methyl pyruvate: –◇–, methyl acetate: –Δ–. Oxidative esterification of 1,2-propanediol with the use of 1% Au/TiO_2. Methanol : 1,2-propanediol was 59 : 1, Au : 1,2-propanediol was 1 : 56. $T = 373$ K, $p(O_2) = 5.0$ bar. 10% $NaOCH_3$ relative to 1,2-propanediol is used.

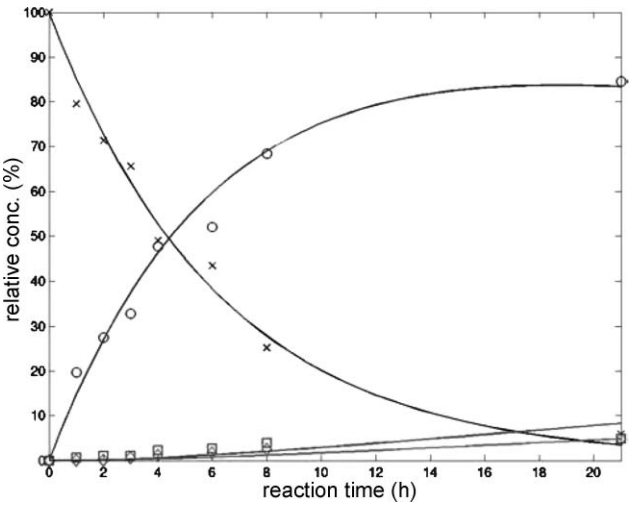
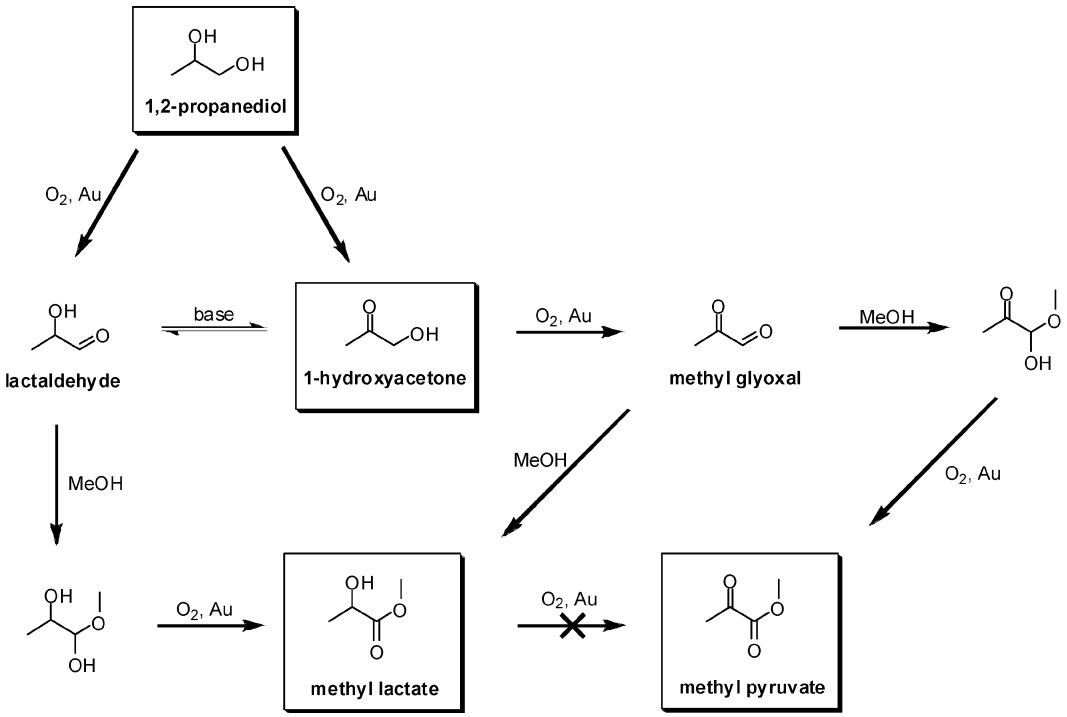


Fig. 4 1,3-Propanediol: –×–, methyl-3-hydroxypropionate: –○–, methyl acrylate: –□–, dimethyl malonate: –◇–. Oxidative esterification of 1,3-propanediol with the use of 1% Au/TiO_2. Methanol : 1,3-propanediol is 59 : 1, Au : 1,3-propanediol was 1 : 112. $T = 373$ K, $p(O_2) = 5.0$ bar. 10% $NaOCH_3$ relative to 1,3-propanediol is used.

1-hydroxyacetone, seemingly being formed at comparable rates. After 21 hours, conversion of 1,2-propanediol is >98% and the selectivity to methyl lactate is 72%. The major by-product after this period of time is methyl acetate, formed with 21% selectivity.

Prati and Rossi performed a detailed examination of the reaction pathway when oxidizing 1,2-propanediol over Au/C in water in the presence of base.[13] They conclude that sodium lactate is stable under oxidative conditions, and that 1-hydroxyacetone yields sodium lactate upon oxidation. Finally, they conclude that methyl glyoxal *via* an intramolecular Canizzaro reaction can be transformed into sodium lactate under basic conditions and that this, together with oxidation of lactaldehyde are two possible intermediates on the route from 1,2-propanediol to sodium lactate.



Scheme 2 Reaction scheme for oxidative esterification of 1,2-propanediol in the presence of base. The observed products are highlighted in boxes.

When oxidizing 1,2-propanediol in methanol, we observed no lactaldehyde, suggesting that either it is an intermediate that is rapidly oxidized into methyl lactate, or that the tautomerisation equilibrium is shifted far towards 1-hydroxyacetone. 1-Hydroxyacetone itself is consumed relatively slowly from the reaction mixture. 1-Hydroxyacetone and lactalaldehyde are tautomers, and are thus in equilibrium under the basic reaction conditions (Scheme 2), hence 1-hydroxyacetone is a likely intermediate on the path to methyl lactate. To confirm the plausibility of this reaction pathway, 1-hydroxyacetone was oxidized under identical conditions to 1,2-propanediol. It was confirmed that methyl lactate was formed (46% selectivity), however large amounts of methyl pyruvate (16% selectivity) and methyl acetate (21% selectivity) were also formed at 86% conversion. The selectivity towards these two by-products was found to be greater than when the starting material is 1,2-propanediol. Oxidation of pure methyl lactate under identical conditions yielded only trace amounts of methyl pyruvate and methyl acetate. It has been reported by Sasaki and co-workers that methyl glyoxal in methanol can be converted into methyl lactate in the presence of various metal chlorides and even in the absence of catalysts.[32] It therefore seems likely that hydroxyacetone can be converted into methyl lactate in two ways in methanol, either *via* tautomerisation to lactaldehyde or *via* oxidation to methyl glyoxal.

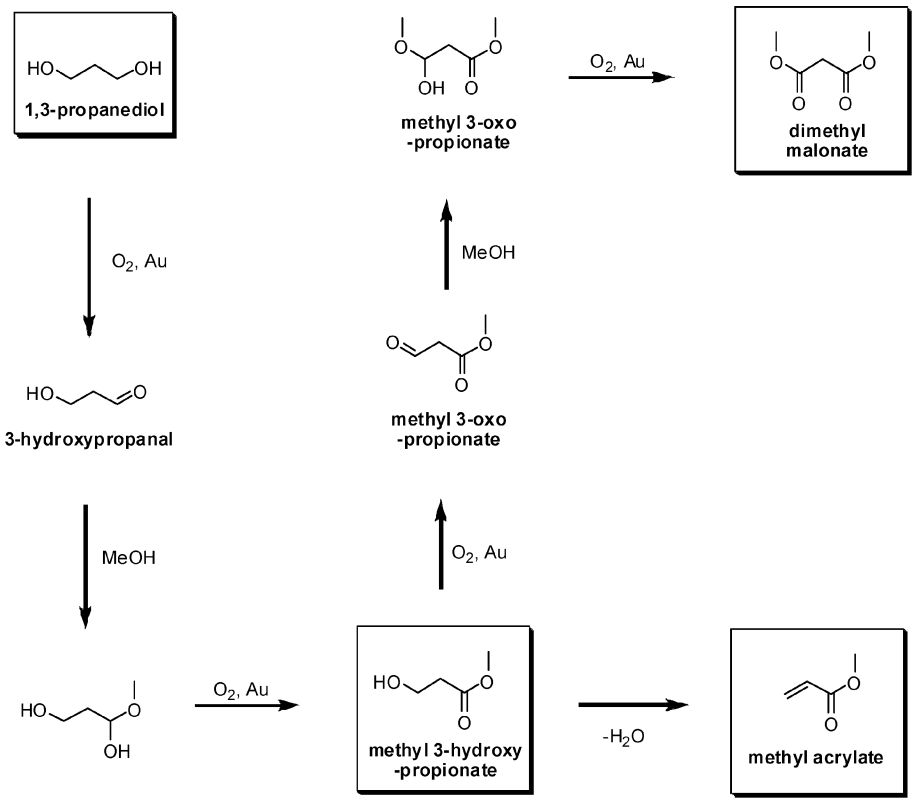
It thus seems plausible that the reaction pathway first involves oxidation of 1,2-propanediol to either lactaldehyde or 1-hydroxyacetone. Lactaldehyde is then oxidized rapidly to give exclusively methyl lactate, whereas 1-hydroxyacetone can give either methyl lactate or methyl pyruvate. This explains the higher selectivity of methyl lactate when oxidizing 1,2-propanediol than when oxidizing 1-hydroxyacetone. Based on the experimental data, it seems reasonable to assume that the majority of methyl pyruvate originates from the oxidation of 1-hydroxyacetone. Methyl pyruvate then undergoes C–C cleavage to form methyl acetate. Cleavage of methyl pyruvate is likely to be the result of peroxides present, as a retro aldol reaction does not seem to be a plausible cause for this reaction.

Thus, these results are consistent with the conclusions drawn by Prati and Rossi from the oxidation of 1,2-propanediol in water.

Oxidation of 1,3-propanediol

Oxidative esterification of 1,3-propanediol in methanol over a supported gold catalyst has already been reported by Hayashi *et al.*[27] However, in order to compare this substrate with glycerol and 1,2-propanediol we examined the oxidative esterification for this substrate as well. We found that 1,3-propanediol is oxidized at a similar rate as glycerol (Fig. 4). Prati and Rossi have reported that diols containing two secondary alcohol groups such as 2,3-butanediol are inert towards oxidation.[13] This points to the simple conclusion that oxidation of polyols with gold catalysts preferentially occurs at a primary alcohol group. Thus, when a substrate contains more than one primary alcohol group, it is more rapidly oxidized.

Oxidation of 1,3-propanediol results in a highly selective formation of methyl 3-hydroxypropionate, with a selectivity of 90% after 21 hours and 94% conversion. Interestingly, only small amounts of oxidation of the second alcohol functionality is taking place. This chemoselectivity indicates that the second alcohol group is influenced by the presence of a methyl ester group 3 carbon atoms away, thus rendering it more difficult to oxidize. Small amounts of oxidation do take place, however,



Scheme 3 Reaction scheme for oxidative esterification of 1,3-propanediol in the presence of base. The observed products are highlighted in boxes.

resulting in the formation of 5% dimethyl malonate. Methyl acrylate is also formed in small amounts (5%) after 21 hours, as a result of dehydration of methyl 3-hydroxypropionate (Scheme 3).

Conclusions

Gold catalyzed oxidative esterification of glycerol, 1,2-propanediol and 1,3-propanediol has been examined and found to be a possible route to important large scale chemicals such as methyl lactate and methyl acrylate. Furthermore, dimethyl mesoxalate can be obtained in high yields directly from glycerol, and potentially directly from the waste steam from biodiesel production.

The oxidation pathway from 1,2-propanediol to methyl lactate has been examined. The pathway was found to be similar to that of oxidation in water over gold catalysts by Prati and Rossi.[13]

The major by-products formed arise from C–C cleavage of C3 products and intermediates. This is likely caused by the presence of hydrogen peroxide. Indeed, using a catalyst that is efficient at breaking down hydrogen peroxide resulted in an increase of the selectivity of dimethyl mesoxalate from 79% to 89%.

The gold catalysts used in this work are significantly less active than the carbon supported gold catalysts reported for the oxidation of aqueous glycerol. A thorough comparison of the reaction rates of glycerol oxidation in water and methanol is necessary in order to draw firm conclusions on the catalytic activity in methanol.

Acknowledgements

The Center for Sustainable and Green Chemistry is sponsored by the Danish National Research Foundation.

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Sustainable Chemistry

DOI: 10.1002/anie.200((will be filled in by the editorial staff))

Zeolite-catalyzed Isomerisation of Triose Sugars**

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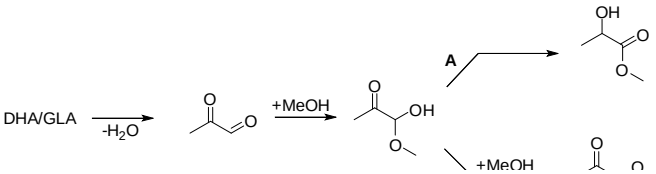
((Dedication----optional))

Lactic acid is an important chemical that is used for production of biodegradable polymers and solvents. The industrial production of lactic acid is based on the anaerobic fermentation of glucose using microbial fermentation.[1] The major complications associated with this process are the need to neutralize lactic acid with a stoichiometric amount of base during the fermentation process and the energy intensive work-up of lactic acid from the aqueous fermentation broth. A different route to lactic acid based on the isomerisation of the triose sugars dihydroxyacetone (DHA) and glyceraldehyde (GLA) could be envisioned, though. Such a process could be based on glycerol as a raw material which by fermentation[2] or catalytic oxidation[3] can be converted to GLA and DHA, respectively.

Herein, we report that Lewis acidic zeolites such as Sn-Beta are highly active and selective catalysts for the isomerisation of trioses to lactic acid, and for the formation of lactate esters. We also demonstrate the importance of the Lewis acidity and Brønsted acidity of the catalyst on the product selectivity and propose that the isomerisation reaction involves a Meerwein-Ponndorf-Verley reduction and Oppenauer oxidation type (MPVO-type) redox step.

Isomerisation of DHA and GLA into lactic acid is energetically favoured by 24 and 27 kcal/mol, respectively.[4] Aqueous acid[5] and base[6] are known to catalyze this isomerisation reaction at temperatures of 250-300 ºC to give moderate yields of lactic acid while aqueous zinc sulphate is known to form up to 86% lactic acid under similar conditions.[7] The isomerisation reaction has also been reported to occur in alcohol solvents, where the resulting product becomes the corresponding lactate ester rather than lactic acid. In methanol, $SnCl_4$ was demonstrated[8] to give up to 89% methyl lactate from DHA at 90 ºC, although in this case large amounts of $SnCl_4$ are needed to achieve high yields. Heterogeneous catalysts have also been employed for this reaction.[9] Thus, Janssen reported that acidic Y-zeolites catalyze the isomerisation-esterification reaction of DHA in ethanol to give moderate yields of ethyl lactate along with some pyruvaldehyde diethylacetal.



Scheme 1. Conversion of DHA in methanol to form either methyl lactate or pyruvaldehyde dimethylacetal (PADA).

The reaction of DHA in alcohols is believed[8-9] to proceed via dehydration to form pyruvaldehyde, followed by conversion to either pyruvaldehyde dimethylacetal (PADA) or methyl lactate (Scheme 1). The formation of methyl lactate (pathway A) necessitates a redox step to be a part of the reaction pathway. We therefore hypothesized that a high selectivity towards methyl lactate is favoured by zeolites that feature redox activity. This particular redox reaction bears a distinct resemblance to the MPVO-redox reaction in which a ketone or an aldehyde is reduced by an alcohol in the presence of a Lewis acidic catalyst.[10] We therefore decided to investigate the activity of zeolites that are known to be highly active MPVO-redox catalysts, for the conversion of DHA to methyl lactate and lactic acid. Such catalysts comprise amongst others extra-framework-aluminum (EFAL) containing zeolites,[11] but more

Table 1. Conversion of dihydroxyacetone to methyl lactate in methanol and to lactic acid in water using various catalysts.[a]

Catalyst	Si/Me ratio[b]	Surface area (m^2/g)	Micro-pore vol. (ml/g)	Methyl lactate (%)	Lactic acid (%)
Al-Beta	65	478	0.19	0	22
Zr-Beta	125	506	0.20	1	44
Ti-Beta	125	492	0.20	2	25
Sn-Beta	125	478	0.19	>99	90
Sn-Beta[c]	125	478	0.19	>99	90
Si-Beta	-	462	0.19	0	3
Al_2O_3/Beta	125	460	0.19	0	8
ZrO_2/Beta	125	453	0.19	0	13
TiO_2/Beta	125	464	0.19	0	11
SnO_2/Beta	125	458	0.19	<1	8
Acidic resin[d]	-	-	-	<1	11
No catalyst	-	-	-	0	3

[a] 1.25 mmol DHA in 4 g of methanol (80 ºC) or water (125 ºC), 80 mg catalyst is added and the mixture is stirred for 24 hours. [b] as synthesized. [c] GLA used as substrate. [d] DOWEX® 50WX8-100.

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[**] The Center for Sustainable and Green Chemistry is sponsored by the Danish National Research Foundation. R.M. West funding by PIRE, NSF OISE 0730277.

interestingly, non-Brønsted acidic zeolites containing framework titanium,[12] zirconium[13] and tin[14] have also been reported to be highly active MPVO-redox catalysts.

We synthesized a series of Beta zeolites containing Al, Zr, Ti and Sn to evaluate their relative activity and selectivity for the reaction of DHA in methanol as well as pure siliceous Beta for comparison (Table 1). Additionally, we prepared the corresponding oxides by incipient wetness impregnation in order to evaluate the importance of framework incorporation of the metals.

The results clearly show that Sn-Beta is a superior catalyst for the conversion of DHA in both methanol and water. The TON calculated per tin-atom is >100 for the conversion of DHA and GLA to methyl lactate. Full conversion of DHA was achieved in water for all zeolites, however only Sn-Beta gave full conversion of DHA in methanol. It was possible to reuse the Sn-Beta catalyst in methanol for 3 consecutive runs without any noticeable loss in activity by simply adding fresh DHA after the 24 hours reaction. However in water this was not possible as large amounts of carbonaceous deposits were formed, resulting in a decrease in the formation of lactic acid from 90% in the first run to 21% in the second run. This could be a result of the unavoidable presence of Brønsted acid in the aqueous reaction mixture, as the concentration of lactic acid increase. Indeed, using a purely Brønsted acidic catalyst such as an acidic ion exchange resin in water, only 11% of lactic acid is formed along with large amounts of carbonaceous deposits.

Besides the obvious advantage of using a heterogeneous catalyst in terms of its reusability, it is interesting to note that when tin is incorporated into the zeolite framework it becomes more active than homogeneous tin in the form of $SnCl_4 \cdot 5H_2O$. Thus, the TOF for the formation of methyl lactate using Sn-Beta is 60 per tin-atom in the first hour whereas it was only 24 using a similar amount of $SnCl_4 \cdot 5H_2O$ as the molar amount of tin in the Sn-Beta catalyst. Additionally, SnO_2/Si-Beta was found to give only trace amounts of methyl lactate although the material contains the same amount of tin as the Sn-Beta zeolite.

This singular site enhancement that is achieved by incorporating tin into the zeolite framework has been studied previously, and the catalytically active site is believed to be a partially hydrolyzed framework tin-specie.[15] The Lewis acid strength of the metal site in the zeolite framework can be evaluated by its ability to shift the carbonyl stretching frequency of cyclohexanone in IR. We found that the C=O-stretch of cyclohexanone shifts by 49 cm^{-1} for the Sn-Beta catalyst, 29 cm^{-1} for Zr-Beta and 22 cm^{-1} for and for Ti-Beta. These results clearly indicate that Sn-Beta is a stronger Lewis acid than Ti-Beta and Zr-Beta, which could explain its increased activity relative to the other metals.

In methanol, the acidic ion exchange resin was found to be highly selective towards PADA. In order to study the selectivity difference for the formation of methyl lactate and PADA, a reaction series was performed at a higher temperature (115 ºC), where all the catalysts are appreciably active. The methyl lactate and PADA yields achieved using the various catalysts are shown in figure 1. Here, it is seen that the acidic ion exchange resin is highly selective towards the formation of PADA (pathway B, scheme 1) whereas Sn-Beta, Zr-Beta and Ti-Beta are only selective for the formation of methyl lactate (pathway A, scheme 1). Al-Beta is highly selective towards PADA, suggesting that it mainly contains Brønsted acidic framework aluminum. In order to substantiate this argument, we decided to steam-dealuminate the Al-Beta zeolite from Table 1 for comparison. Hence, the Al-Beta was steam calcined at 750 ºC for 20 hours. Here it was found that the selectivity towards methyl lactate increases significantly, as would be expected from the formation of more EFAL sites (Figure 1).

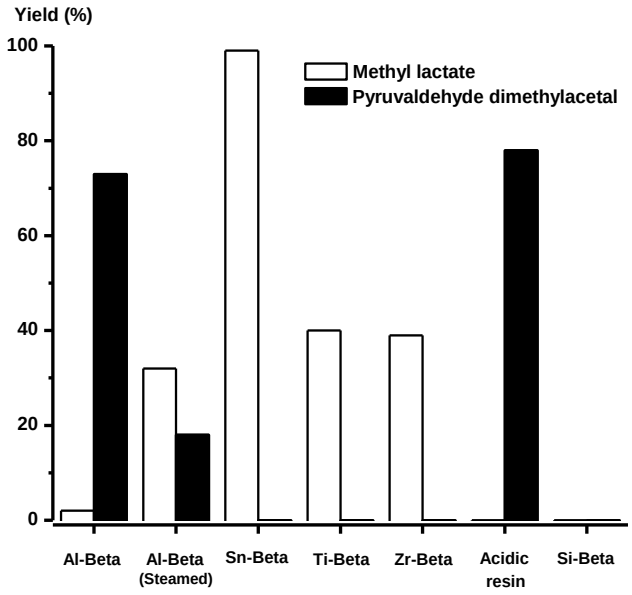

Figure 1. Yield of methyl lactate and PADA for various catalysts. Conditions: DHA (1.25 mmol), methanol (4 g) and catalyst (80 mg) was stirred at 115 ºC for 24 hours.

It is thus clear that for the reaction of triose sugars in methanol, Lewis acidic catalysts are selective towards the formation of methyl lactate, whereas Brønsted acidic catalysts are selective towards PADA. The zeolite activity correlates with its relative Lewis acid strength as determined by IR-measurement of adsorbed cyclohexanone. The reaction pathway could be thought to involve a MPVO-type redox reaction of the pyruvaldehyde hemiacetal (MeOH) or hydrate (H_2O) in which a 1,2-hydride shift takes place in a concerted fashion leading to methyl lactate or lactic acid, respectively (scheme 2).

Scheme 2. Tentative MPVO-type redox reaction leading to methyl lactate.

The strongly Lewis acidic Sn-Beta catalyst used here is to the best of our knowledge the most active catalyst reported until now for the conversion of triose sugars to methyl lactate and lactic acid. It is more active than even homogeneous tin chloride, and due to its ease of reuse it is more attractive from an environmental point of view. The excellent activity, selectivity and reusability illustrate the important potential that zeolites have in the conversion of biomass to value added chemicals.

Experimental Section

Sn-Beta, Zr-Beta, Ti-Beta, Al-Beta, Si-Beta were all synthesized in fluoride media according to known procedures. The metal oxides on Si-Beta were prepared by incipient wetness impregnation using corresponding metal precursers and then calcined at 450 ºC for 4 hours.

In a 15 mL Ace-vial, 1.25 mmol of substrate (DHA or GLA), 4.0 g of solvent (MeOH or H_2O) and 80 mg of catalysts were added. In the case of MeOH, 60 mg naphthalene was also added as an internal standard. The vials were then immersed into a preheated oilbath and stirred for 24 hours. Reactions performed with MeOH as solvent were analyzed by GC and HPLC and reactions performed with H_2O as solvent were analyzed by HPLC.

Received: ((will be filled in by the editorial staff))
Published online on ((will be filled in by the editorial staff))

Keywords: heterogeneous catalysis · trioses · tin · Lewis acidic zeolites · lactic acid

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